1/123

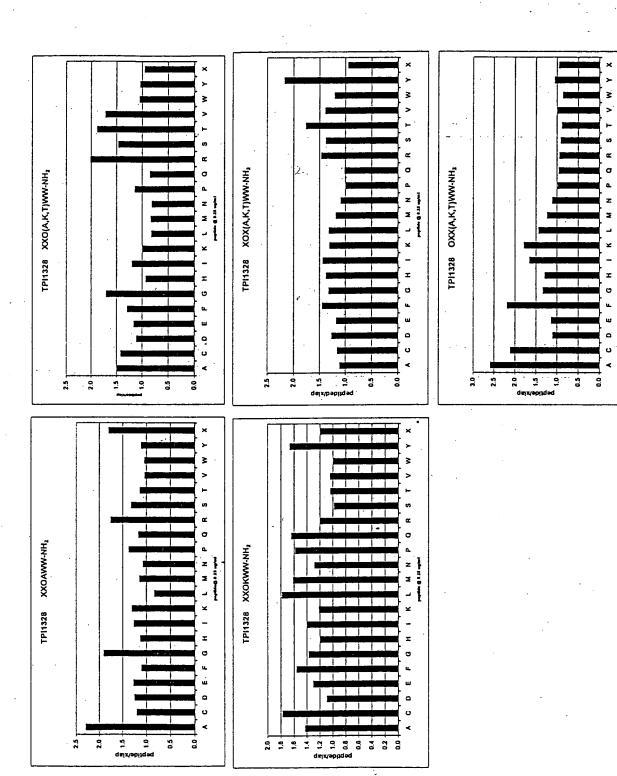


FIGURE 1

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TPI 1313

	4						•			
	1 L-Thiala	2	3 ′	4					مسيدان بالمرابع فيعموم الراء المرابية فياد	
	D-Thiala	D-pCl-Phe D-OEt-Tyr	D-OEI-Tyr	D-pCI-Phe					Ratio>1945	
	Phe	D-OE(-1y) D-Phe	D-Nai	D-pNO2-Phe D-Thiala						
	7 110	D-I lie		U-Illiala			Ratio		Ratio	
							Caspase3/Xiap		peptide/xiap	
Vial#	1	2	3	4			Avg	std	AVG	std
1	L-Thiala	D-pCI-Phe	D-OEI-Tyr	D-pCl-Phe	-NH2		0.9	0.036	1.3	0.20
2	L-Thiala	D-pCI-Phe	D-OEI-Tyr	D-pNO2-Phe	-NH2		0.9	0.035	1.3	0.22
3	L-Thiala	D-pCI-Phe	D-OEt-Tyr	D-Thiala	-NH2		0.9	0.031	0.9	0.10
. 4	L-Thiala	D-pC1-Phe	D-Nal	D-pCI-Phe	-NH2		0.9	0.031	2/3	0.60
5	L-Thiala	. D-pC!-Phe	D-Nal	D-pNO2-Phe	-NH2		0.9	0.033	2172	0.24
6	L-Thiala	D-pCI-Phe	D-Nai	O-Thiala	-NH2		0.9	0.029	1.3	0.17
7	L-Thiala.	D-QEt-Tyr	D-OEt-Tyr	D-pCI-Phe	-NH2		0.9	0.024	2:7	0.37
8	L-Thiala	D-OEI-Tyr	D-OEt-Tyr	D-pNO2-Phe	-NH2		0.9	0.027	1.4	0.21
9	L-Thiala	D-OEt-Tyr	D-OEt-Tyr	O-Thiala	-NH2		0.9	0.032	0.9	0.05
10	L-Thiala	D-OEt-Tyr	D-Nal	D-pCl-Phe	-NH2		0.9	0.029	0.7	0.09
,11	L-Thiala	D-OEt-Tyr	D-Nal	· D-pNO2-Phe	-NH2		0.9	0.031	0.9	0.18
12	L-Thiala	D-OEt-Tyr	D-Nal	O-Thiala	-NH2		0.9	0.029	0.9	0.13
13	L-Thiala	D-Phe	D-OEt-Tyr	0-pCI-Phe	-NH2		0.9	0.028	0.6	0.08
14	L-Thiala	D-Phe	D-OEt-Tyr		-NH2		0.9	0.028	0.6	80.0
15	L-Thiala	D-Phe	D-OEt-Tyr	D-Thiala	-NH2		0.9	0.025	0.6	0.07
16 17	L-Thiala	D-Phe	D-Nai	D-pCI-Phe	-NH2		0.9	0.029	0.8	0.09
18	L-Thiala L-Thiala	D-Phe	D-Nai	D-pNO2-Phe	-NH2		0.9	0.032	1.1	0.10
19	O-Thiala	D-Phe D-pCI-Phe	D-Nai	D-Thiala	-NH2		0.9	0.029	0.9	80.0
20	D-Thiala D-Thiala	D-pCI-Phe	D-OEt-Tyr D-OEt-Tyr	D-pCI-Phe	-NH2		0.9	0.031	1.5	0.24
21	D-Thiala	D-pCI-Phe	D-OEI-Tyr	D-pNO2-Phe D-Thiala	-NH2		0.8	0.042	1.3	0.30
22	D-Thiala	D-pCI-Phe	D-Nai	D-pCi-Phe	-NH2 -NH2		0.9 0.9	0.030	0.9	0.10
23	D-Thiala	D-pCI-Phe	D-Nai		-NH2		0.9	0.030 0.022	1.0	0.14
24	D-Thiala	D-pCI-Phe	D-Nal	D-Thiala	-NH2		0.9	0.022	1.0 1.3	0,10
25	D-Thiala	D-OEt-Tyr	D-OEt-Tyr		-NH2		1.0	0.024	1.5	0.16 0.20
26	D-Thiala	D-OEt-Tyr	D-OEt-Tyr		-NH2		0.8	0.027	1.1	0.20
27	O-Thiala	D-OEt-Tyr	D-OEt-Tyr	D-Thiala	-NH2		0.9	0.037	1.1	0.12
28	D-Thiala	D-OEt-Tyr	D-Nai	D-pCl-Phe	-NH2		0.9	0.041	1.1	0.11
29	O-Thiala	D-OEI-Tyr	D-Nai	D-pNO2-Phe	-NH2		0.9	0.032	1.1	0.14
30	D-Thiala	D-OEt-Tyr	D-Nal	D-Thiala	-NH2		0.9	0.043	1.2	0.12
31	D-Thiala	D-Phe	D-OEt-Tyr	D-pCI-Phe	NH2		0.9	0.038	1.3	0.15
32	O-Thiala	D-Phe	D-OEt-Tyr	D-pNO2-Phe	-NH2		1.0	0.036	1.1	0.08
33	O-Thiala	D-Phe	D-OEt-Tyr	D-Thiala	-NH2		0.9	0.034	1.0	80.0
. 34	D-Thiala	O-Phe	D-Nai	D-pCI-Phe	-NH2		0.9	0.027	1.0	0.13
35	D-Thiala	D-Phe	D-Nai	D-pNO2-Phe			0.9	0.029	0.9	0.12
36 27	D-Thiala	D-Phe	D-Nal	O-Thiala	-NH2		0.9	0.032	1.1	0.13
37 - 38	Phe Phe	D-pCI-Phe	D-OEt-Tyr	D-pCI-Phe	-NH2	٠	0.9	0.042	1.3	0.14
39	Phe	D-pCI-Phe D-pCI-Phe	D-OEt-Tyr	D-pNO2-Phe			0.9	0.030	0.8	0.12
40	Phe	D-pCI-Phe	D-OEt-Tyr	D-Thiala	-NH2	•	0.9	0.029	0.9	0.11
41	Phe	D-pCI-Phe	D-Nai D-Nai	D-pCI-Phe D-pNO2-Phe	-NH2 -NH2		0.9 1.0	0.026	199	0.13
42	Phe	D-pCI-Phe	D-Nai	D-Thiala	-NH2		0.9	0.120	0.9	0.07
43	Phe	D-OEt-Tyr	D-OEt-Tyr	D-pCl-Phe	-NH2		1.0	0.045 0.098	1.0 0. 9	0.27
44	Phe	D-OEt-Tyr	D-OEt-Tyr	D-pNO2-Phe			1.0	0.139	1.0	0.14
45	Phe	D-OEI-Tyr	D-OEt-Tyr	D-Thiala	-NH2		1.0	0.114	0.8	0.07 0.23
46	Phe	D-OEt-Tyr	D-Nal	D-pCI-Phe	-NH2		1.0	0.124	0.9	0.26
47	Phe '	D-OEt-Tyr	D-Nai		-NH2		0.9	0.100	1.0	0.23
48	Phe	D-OEt-Tyr	D-Nal	D-Thiala	-NH2		1.0	0.068	1.0	0.05
49	Phe	D-Phe	D-OEt-Tyr	D-pCI-Phe	-NH2		1.0	0.057	1.1	0.09
. 50	Phe	D-Phe	D-OEI-Tyr	D-pNO2-Phe	-NH2		0.9	0.106	0.9	0.07
51	Phe	0-Phe	D-OEI-Tyr	D-Thiala	-NH2		1.0	0.056	- 0.9	0.03
52	Phe	D-Phe	D-Nai	D-pCl-Phe	-NH2		0.9	0.083	1.0	0.14
53	Phe	D-Phe	D-Nai	D-pNO2-Phe	-NH2		0.9	0.080	0.9	0.06
54	Phe	D-Phe	D-Nai	D-Thiala	-NH2		1.0	0.127	0.9	0.03

C₄₀H₄₂CIN₄ Exact Mass

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CI

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058

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31. 32. H_2N H_2N) O 0 C₃₆H₄₀N₅O₇S Exact Mass: 7 $C_{36}H_{40}CIN_5O_5S$ Exact Mass: 689.24 CI O₂N 33. H_2N H_2N 0 0 MO H C₃₄H₃₉N₅O₅S₂ Exact Mass: 661.24 C₃₈H₃₈CIN₅O, Exact Mass: 6 35. 36. H_2N H_2N 0 Ó C₃₆H₃₇N₅O₄S Exact Mass: 6 C₃₈H₃₈N₆O₆S Exact Mass: 706.26 O_2N 37. 38. H_2N NH_2 0 0 0 0 C₃₈H₄₁CIN₅O₇ Exact Mass: 72 C₃₈H₄₁Cl₂N₅O₅ Exact Mass: 717.25 O_2N Cl CI .CI 39. 40. $H^{5}N$ NH₂ Ĭ O) | | |)II O ö C₄₀H₃₉Cl₂N₅O₄ Exact Mass: 721 C₃₆H₄₀CIN₅O₅S Exact Mass: 689.24 CI

CI

JO

 \int_{0}^{∞}

C₃₈H₃₉N₅O₄S Exact Mass: 6

 H_2N

 O_2N

Ĭ

 $C_{40}H_{40}N_6O_6$ Exact Mass: 700.30

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058

9/123

Define functionalities of most active mixtures of N-Acyl triamine library (TPI 914)

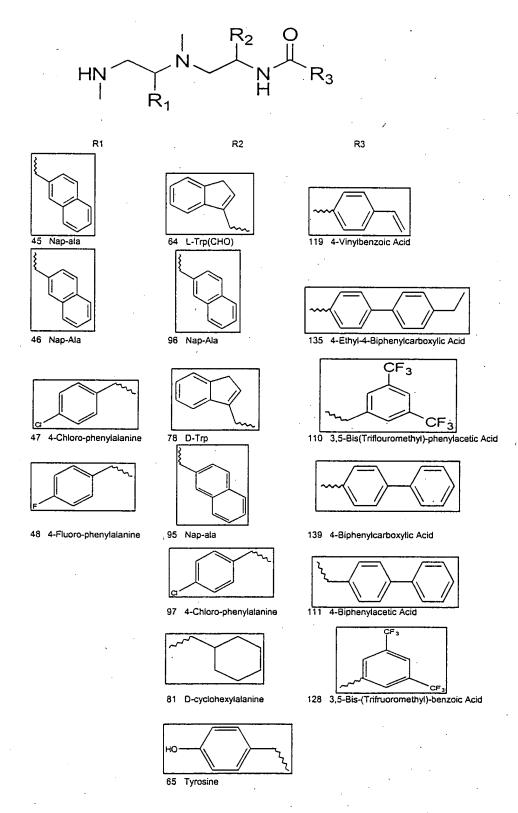


FIGURE 4

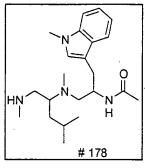
Title: METHODS AND COMPOSITIONS FOR...
Inventors: Reed et al.
Filed: Herewith

Docket No.: 66821-058

10/123

TPI 914 Controls

#	R1	R2	R3	Lowest concentration with Ratio of ~ 2.0
178	L-Leu	D-Trp	CH3	12.5 ug/ml
210	L-Leu	L-Phe	3,5-Bis(Trifluoromethyl)-Phenylacetic Acid	6.25 ug/ml
219	L-Leu	L-Phe	4-Vinylbenzoic Acid	6.25 ug/ml
235	L-Leu	L-Phe	4-Ethyl-4-Biphenylcarboxylic Acid	6.25 ug/ml
				•



TPI 927

FIGURE 6

Filed: Herewith
Docket No.: 66821-058

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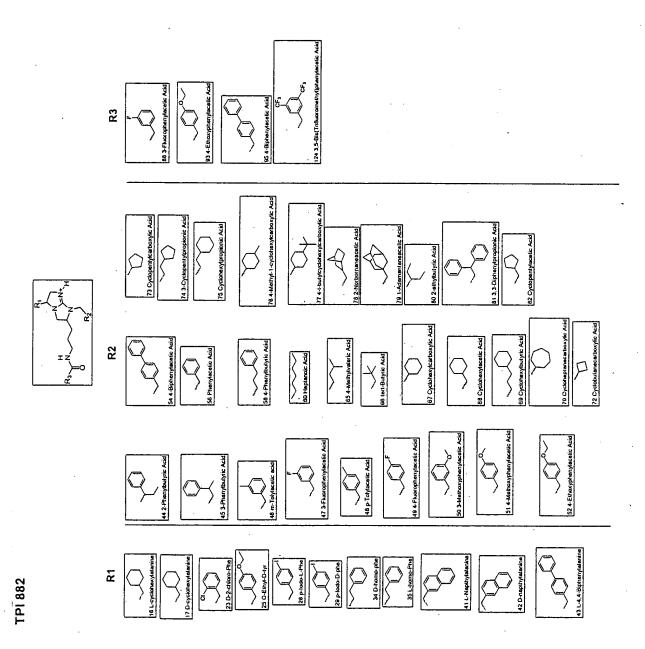
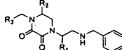


FIGURE: 7

TPI 759 N-Benzyl-1,4,5-trisubstited-2,3-diketopiperazines



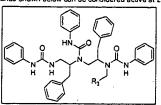
		O R, "				•				
Selections	22 Fn 25 Fn 29 Fn 28 Fn 5 Fn 24 Fn 23 Fn	noc-Nie noc-nie noc-NapAla noc-ChAla noc-Lys(Box noc-nva noc-nva noc-val	R2 43 Fmoc 52 Fmoc 41 Fmoc 31 Fmoc 33 Fmoc 46 Fmoc 34 Fmoc	-NapAla -phe -Phe -ile -lle -val	60 87 58 66 89 90 81 61	4-Isobutyl-alpha-N 3,5-Bis(Trifluorom Heptanoic Acid (Alpha-Alpha-Alph 4-tert-Butyl-cycloh m-Totylacetic Acid 3,4-Dichlorophenyl 3,3-Diphenyl propic Dicyclohexylacetic Cycloheptanecarbc p-Totylacetic Acid Cyclohexanebutyric	ethyl)-Phenylacetic a-Trifluoro-m-Tolyl exanecarboxylic A acetic Acid onic Acid acid axylic Acid	Acid) acetic acid		
	R1		R2		R3					
21 Nort	leucine	43 lev	cine	65 4-	Isobutyl-a	sipha-methylphenyl	acetic acid	1	81 Cycloheptanecai	rbox
22				ا ا	Ţ					ل
22 norte		52 Na	envlalan	ام.	eptanoic a	acid	lacetic acid		61 P. Tolylacetic acid	\
29 cyck	ohexylalani	31 Phe	enylalar	60 (A	Jpha-alph	ia-alpha-trifluoro-m-	tolyl)acetic acid			
28 Cycl	lohexylalan	42 isol	eucine	87 4-1	tert-Butyl-	cyclohexanecarbox	rylle acid			•
5 Lysir	ne .	33 Isol	eucine	58 m-	tolylaceti	c acid				
24 norv	aline	46 vali	ne	66 3,4	4-Dichloro	CI ophenylacetic acid				
23 Narv	valine	34 Leu	cine	89 3,3	3-Dipheny	/propionic acid		·		
19 valin	le le			90 Die	cyclohexy	dacetic acid				

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058

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TPI 927 controls

Most of the compounds shown below can be considered active at 25 ug/ml



116 Trimethylacetic Acid 119 Cyclohexylacetic Acid 109 Hydrocinnamic Acid 102 3-Methoxyphenylacetic Acid 111 Butyric Acid 127 4-tert-Butylcyclohexanecarboxylic Acid 133 3-(3,4,5)-Trimethoxyphenylpropionic Acid 126 4-Methy-1-Cyclohexanecarboxylic Acid 112 Heptanoic Acid 130 Cyclopentylacetic Acid 2-Norbornaneacetic Aci 125 Cyclohexanepropionic Acid 118 Cydonexanecarboxylic Acid 117 tert-Butyl acetic Acid 108 Phenylacetic Acid 104 4-Ethoxyphenylacetic Acid 121 Cycloheptanecarboxylic Acid 129 3,3-Diphenylpropionic Acid 123 Cyclobutanecarboxylic Acid 103 4-Methoxyphenylacetic Acid 120 Cyclohexanebutyric Acid 122 Acetic Acid 128 1-Adamantaneacetic Acid 115 4-Methylvaleric Acid 124 Cyclopentanecarboxylic Acid 101 p-Tolylacetic Acid 113 Isobutyric Acid 105 4-isobutyl-alpha-methylphenyla

FIGURE 9

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058 15/123

TPI 882 controls
All the compounds below have activity at 8 ug/ml

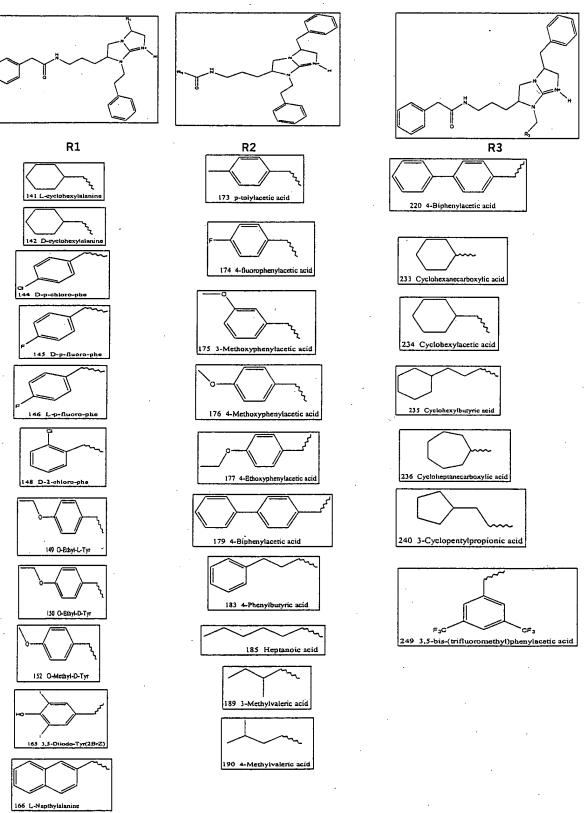


FIGURE 10

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058

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Hexape~1

TPI1239 dose responses (sort)

TPI 1239

All mix are N-terminal free and C-terminal amide

Caspase 3-XIAP

From file 032001-IC50 of selected TPI 1239

Note that Smac is only tested at 1 $\ensuremath{\text{mM}}$

Caspase effect

'								
	2 ug/ml		1ug/ml		0.5 ug/ml		0.25 ug/ml	
	Avg	std	Avg	std	Avg	std	Avg	std
Caspase 3	1.0	0.0	1.0	0.0	1.0	0.0	1.0	0.0
Xiap+C3	0.4	0.0	0.4	0.0	0.4	0.0	0.4	0.0
SMAC	0.9	0.1	0.9	0.1	0.9	0.1	0.9	0.1
XXXAWW	1.0	0.0	1.1	0.0	1.1	0.0	1.0	0.0
XXXHWW	1.0	0.1	1.1	0.0	1,1	0.0	1.0	0.1
XXXKWW	1.0	0.1	1.0	0.0	1.0	0.0	1.1	0.1
XXXNWW	1.0	0.0	1.0	0.0	1.0	0.0	1.0	0.0
XXXQWW	1.0	0.0	1.0	0.0	1.0	0.0	1.0	0.0
XXXRWW	1.0	0.0	1.0	0.0	1.0	0.0	1.0	0.0
XXXSWW	1.0	0.0	1.0	0.0	1.0	0.0	1.0	0.1
XXXTWW	1.1	0.0	1.1	0.0	1,1	0.0	1.0	0.0
xxxvww	1.0	0.0	0.9	0.0	1.0	0.1	1.0	0.0
XXXXWW	1.0	0.0	1.1	0.1	1.0	0.0	1,1	0.0
XIAP effect								
	2ug/ml	Std	1ug/ml	Std	0.5 ug/ml	5td	0.25 ug/ml	Std
Caspase 3	2.2	0.0	2.2	0.0	2.2	0.0	2.2	0.0
Xiap+C3	1.0	0.0	1.0	0.0	1.0	0.0	1.0	0.0
SMAC	2.0	0.1	2.0	0.1	2.0	0.1	2.0	0.1
XXXAWW	2.2	0.0	2.0	0.0	1.7	0.0	1.4	0.0
XXXKWW	2.2	0.1	2.0	0.2	1.6	0.1	1.2	. 0.1
XXXTWW	2.1	0.0	1.8	0.0	1.6	0.0	1.2	0.1
XXXSWW	2.1	0.2	1.8	0.0	1.4	0.1	1.3	0.3
WWWXXX	1.8	0.2	1.4	0.0	1.2	0.1	1.1	0.1
XXXVWW	1.7	0.0	1.4	0.0	1.2	0.2	1.0	0.1
XXXXWW	1.8	0.1	1.4	0.1	1.1	0.1	1.1	0.3
XXXHWW	1.8	0.1	1.4	0.1	1.1	0.1	1.0	0.1
XXXRWW	1.4	0.1	1.1	0.0	1,1	0.1	0.9	0.1
XXXQWW	1.5	0.0	1.3	0,0	1.1	0.1	0.9	0.1

Analysis:

⁻No effect on caspase activity, first block of data.

⁻The most active mixtures from XXXOWW are A, K and T

⁻ The next step of the deconvolution could be a PS-SCL for positions 1,2 and 3, position 4 having A,K,T and positions 5 and 6 as W

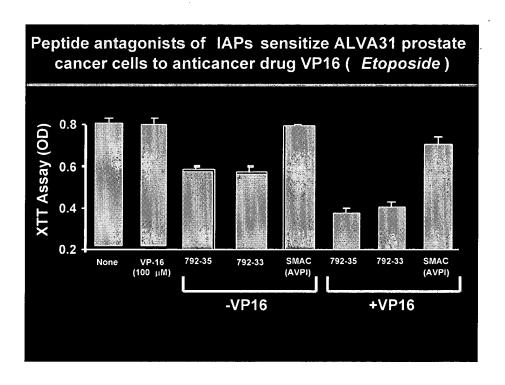
etra-peptide antagonists of XIAP

792-35

Exact Mass: 898.32793

Exact Mass: 1067.46153

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19/123

TPI 1391 N-Benzyl-1,4,5-trisubstited-2,3-diketopiperazines

TPI 1396
Polyphenylureas
Diphenyl or Triphenylureas

FIGURE 14A

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058 20/123

TPI1396-11

Exact Mass: 747.48

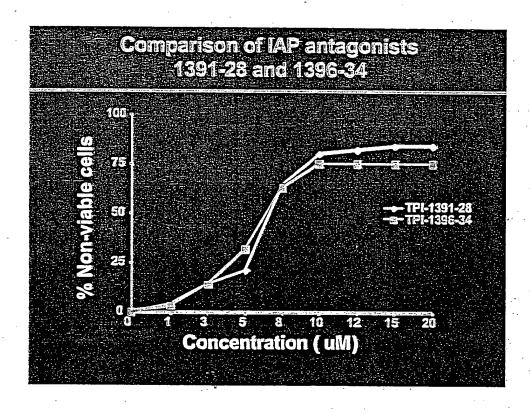
Exact Mass: 655.35

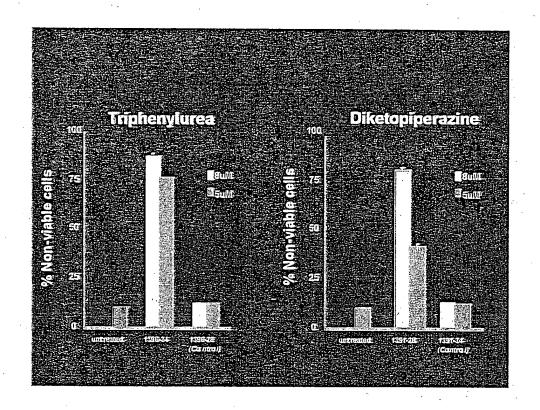
TPI1396-12

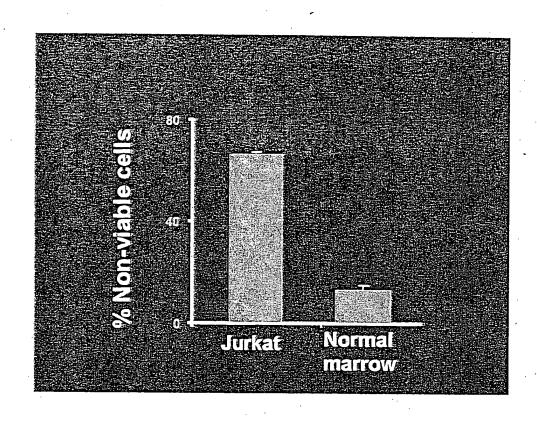
Exact Mass: 723.48

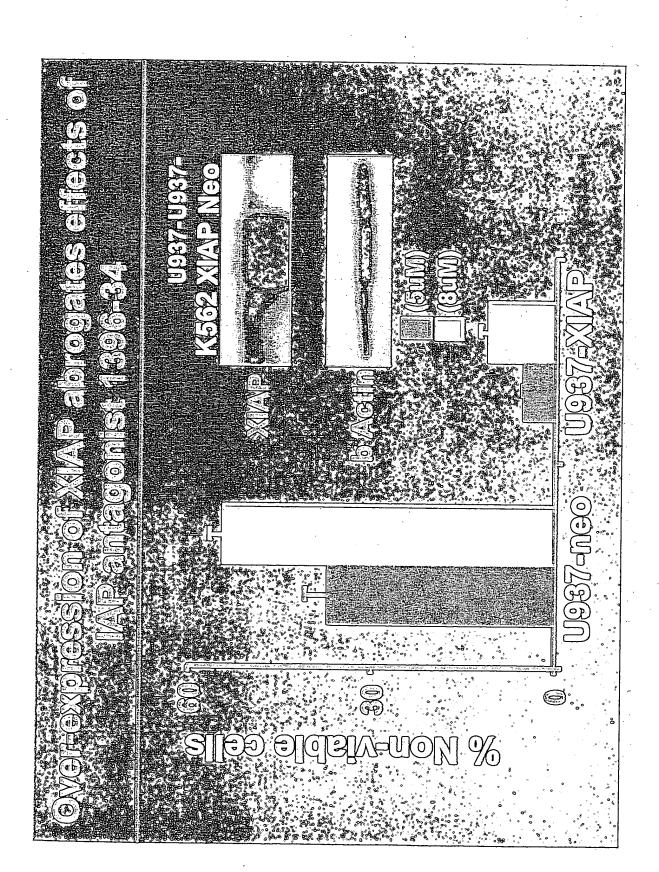
FIGURE 14B

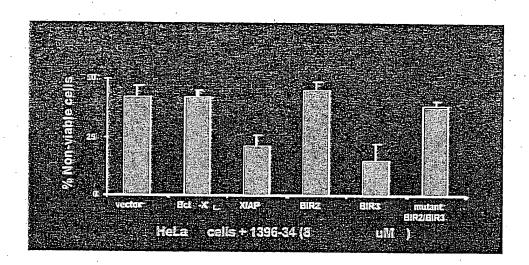
Inventors: Reed et al.
Filed: Herewith
Docket No.: 66821-058
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TP11349	TPI1349 Structures FIGURE 21	MM	Exact Mass	emen	Mt one	HBondAcceptor HBondDonor Bule Office	HBondDonor	P. do Office
-	Boc-D-(2-Naphthyl)-alanine Boc-L-Tryptophan(Formyl) 4-Vinytbenzoie acid	· · · · · · · · · · · · · · · · · · ·	544.3	yy)-1-{(metryl[(1R)-2- l)etryl[amino]metry)etryl}- mide	4.3	vo	2	2
٥.	Boc-D-(2-Naphthyl)-alanine Boc-L-Tryptophan(Formyl) 4-Ehyl-4-Biphenylcarboxylic acid	- 622.9	622.4	4-ethyl-N-[(1S)-2-(1-methyl-1H-indol-3-yl)-1-((methyl[1R)-2- (methylamino)-1-(2-naphthylmethyl]amino)methyl)ethyl]- 1,1-biphenyl-4-carboxamide	5.2	u)	2	. 8
m	(Boc-D-(2-Naphthyt)-alanine)[Boc-L-Tryptophan(Formyt)][3]. SBis-(trifluoromethyt)-phenylacetic acid	668.7	668.3	2-[3,5-bis(trifluoromethyl)phenyl)-N-[(1S)-2-(1-methyl-1H-indo) 3-yl)-1-((methyl(1R)-2-(methylamino)-1-(2- naphthylmethyl)ethyljamino}methyl)ethyljacetamide	5.6	us .	2	8
4		594.8	594.3	N-{(1S)-2-(1-methyl-1H-indol-3-yl)-1-((methyl(1R)-2- (methylamino)-1-(2-naphthylmethyl)amino)methyllethyl)- 1,1-biphenyl-4-carboxamide	o	u)	N	. 8
ဟ		608.8	608.4	2-(1, 1'-biphenyl-4-y0-N-{(15)-2-(1-mathyl-1H-indol-3-yl)-1- ((methyl(1R)-2-(methylamino)-1-(2- naphtylmethyl)ethyljamino)methyl)ethyljacetamide	80.	u)	2	8
ω		541.7	541.3	N-{(1S)-2-(methyl(1R)-2-(methylamino)-1-(2- naphthylmethyl)ethyljamino}-1-(2-naphthylmethyl)ethyl]-4- vinylbenzamide	5. 6.	. 4	2	٥ .

1	O	/1	1	7
L	o	/ 1	L	J

TP1134	TPI1349 Structures FIGURE 21	MΜ	Exact Mass	Name	MLoaP	MLoaP HBondAcceptor HBondDonor RuleOfFive	HBondDonor	RuleOfFive
	Boc D.(2-Naphthyl)-alanina Boc-L-(2-Naphthyl)-alanina 4-Eiphenylcanboxylic acid	619.8	619.4	r2-(methylamino)-1-(2- naphbylmethyl)ethyll-1,1'- oxamide	25.	4	~	8
ω	Boc-D-(2-Naphthyl)-alanine Boc-L-(2-Naphthyl)-alanine Goc-L-(2-Naphthyl)-alanine Goc-L-(2-Naphthyl)-(2-Naphthyl)-alanine Goc-L-(2-Naphthyl)-(2-Naphthyl)-(2-Naphthyl)-(2-Naphthyl)-(2-Naphthyl)-(2		665.3	2-[3.5-bis(ufiluoromethyl)phenyl -N-[(1S)-2-(methyl[(1R)-2- (methylamino)-1-(2-naphthylmethyl)ethyljannino)-1-(2- naphthylmethyljacetamide	6. 6.	4	2	8
on .		591.8	591.3	N-{(1S)-2-(methyl(1R)-2-(methylamino)-1-{2- naphthylmethyl)ethyljamino}-1-{2-naphthylmethyl)ethyl}-1.1'- biphenyl-4-carboxamide	6.2	4	2	. 8
6		605.8	605.3	2-(1,1-biphenyl-4-y)-N-(1S)-2-(methyl(1R)-2-(methylamino)- 1-(2-naphthylmethyl)ethyljamino)-1-(2- naphthylmethyljacetamide	6.1	4	2	۵ .
-	Boc-D-(2-Naphthyl)-alanina Boc-D-Tryptophan 4-Vinytbenzoic acid	544.7	544.3	N-{(1R)-2-(1-methyl-1H-indol-3-yl)-1-{(methyl(1R)-2- (methylamino)-1-(2-naphtydnethyl)ethyl)aminojmethyl)ethyl}- 4-vinylbenzamide	£.	vi	2	8
12	Boc-D-(2-Naphthyr)-elanine Boc-D-Tryplophan 4-Etry+4-Biphenykcarboxylic acid	622.9	622.4	4-ethyl-N-[(1R)-2-(1-methyl-1H-indol-3-yl)-1-((methyl[(1R)-2- (methylamino)-1-(2-naphthylmethyl)ethyl]aminolmethyl)ethyl]- 1,1'-biphanyl-4-carboxamide	5.2	un	7	

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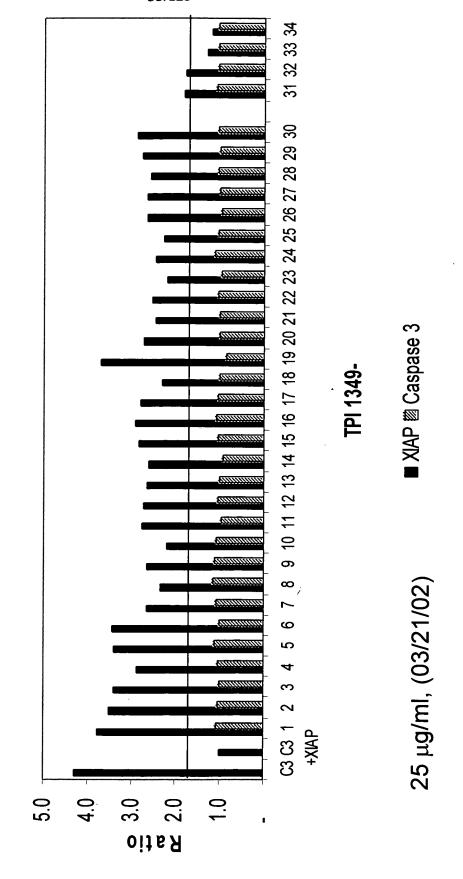
TP11349	TPI1349 Structures FIGURE 21	MW	Exact Mass	Name	MLogP	HBondAcceptor HBondDonor RuleOfFive	HBondDonor	RuleOfFive
£	Grand Caracteristics (Caracteristics) (Goc.D.(2-Naphthyl)-alanine)[Boc.D-Tryptophan]3,5-Bis-(trifluoromethyl)-phenylacetic acid]	668.7	. 668.3	2-[3,5-bis(trifluoromethyl)phenyl-N-{(1R)-2-(1-methyl-1H-indol-3-yl)-1-((methyl(1R)-2-(methylamino)-1-(2-naphthylmethyl)ethyljamino)methyl)ethyljacetamide	I	u	8	7
. 4	Boc.D.(2-Naphihyl)-alanine][Boc.D.Toptophan][4-Biphanytcarboxylic acid]	594.8	594.3	N-[(1R)-2-(1-metryl-1H-indol-3-yl)-1-((metryl((1R)-2- (metrylamino)-1-(2-naphtrylmetryl)etryljaminojmetryl)etrylj- 1,1'-biphenyl-4-carboxamide	6:	va	. 8	٥
15	Boc. D.(2-Naphthyt)-alanine)[Boc. D.Trypttophan[14-Biphenylacetic acid]	608.8	608.4	2-{1,1'-biphenyl-4-yl-N-{(1R)-2-{1-methyl-1H-indol-3-yl)-1- ((methyl(1R)-2-{methylamino}-1-(2- naphtyylmethyl)ethyljamino)methyl)ethyljacetamide	6.	\u00eda	8	0
16	Boc.L.(2-Naphthyl)-alanina Boc.L.Tryptophan(Formyl) 4-Vinybenzoic acid	544.7	544.3	N-[(1S)-2-(1-methyl-1H-indol-3-yl)-1-((methyl(1S)-2. (methylamino)-1-(2-naphthylmethyl)ethylaminojmethyl)ethyll- 4-vinylbenzamide	4.3	vo	N	8
11	Boc.L.(2-Naphthyl)-elenine Boc.L-Tryptophan(Formyl) 4-Eirhyl-4-Biphenylcarboxylic ecid	622.9	622.4	4-ettyk-N-{(1S)-2-(1-mettyl-1H-indol-3-yl)-1-{(mettyl(1S)-2- (mettylamino)-1-(2-naphthylmettyl)ettyl]aminojmettyl)ettyl}- 1.1-biphenyl-4-carboxamide	5.2	us.	8	20
84	Cra Cramphity)-elanine)[Boc-L-Tryptophant[Formyl)][3,5-8is-(trifluoromethyl)-phenylacetic acid		668.3	2-{3,5-bis(trifluoromethyl)phenyl}-N-{(15)-2-(1-methyl-1H-indol: 3-yl)-1-{(methyl(15)-2-(methylamino)-1-{2. naphthylmethyl)ethyllamino)methyl)ethyljacetamide	9 9	v	8	, 8

Boccl-(2-Naphthyt)-atanine) Boccl-(2-Naphthyt)-atanine) Boccl-(2-Naphthyt)-atanine) Boccl-(2-Naphthyt)-atanine) Boccl-(2-Naphthyt)-atanine) Boccl-(2-Naphthyt)-atanine) Boccl-(2-Naphthyt)-atanine) Boccl-(2-Naphthyt)-atanine) Boccl-(2-Naphthyt)-atanine) Boccl-(2-Naphthyt)-atanine) Boccl-(2-Naphthyt)-atanine) Boccl-(2-Naphthyt)-atanine) Boccl-(2-Naphthyt)-atanine) Boccl-(2-Naphthyt)-atanine) Boccl-(2-Naphthyt)-atanine) Boccl-(2-Naphthyt)-atanine) Boccl-(2	TP11346	TPI1349 Shuctures FIGURE 21	MW	Exact Mass	Name	MI ooP	MLooP HBondAcceptor	HBondDonor	RulaOfFiva
[Boc-L-(2-Naphthyt)-alanine][Boc-L-(2-Naphthyt)-alanine][Ac-L-(2-Naphthyt)-alanine][Bo	61	Boc-L-(2-Naphthyl)-alanina Boc-L-Tryptophan(Formyl) 4-Biphenytcarboxylic acid]		594.3	N-[(1S)-2-(1-metryl-1H-indo:-3-yl)-1-((metryl[(1S)-2- (metrylamino)-1-(2-naphtrylmetry)letryl]etryl]etryl]- 1,1'-biphenyl-4-carboxamide	e. 6.		0	, 8
Boc-L-(2-Naphthyt)-alanina Boc-L-(2-Naphthyt)-alanina 4-Vinybenzoic acid Boc-L-(2-Naphthyt)-alanina Boc-L-(2-Naphthyt)-alanina 4-Etryt-4-Biphenyicarboxylic acid Boc-L-(2-Naphthyt)-alanina Boc-L-(2-Naphthyt)-alanina 4-Etryt-4-Biphenyicarboxylic acid Boc-L-(2-Naphthyt)-alanina Boc-L-(2-Naphthyt)-alanina 3-Etis-(trifluoromethyt)-phenylacetic acid Boc-L-(2-Naphthyt)-alanina Boc-L-(2-Naphthyt)-alanina 3-Etis-(trifluoromethyt)-phenylacetic acid	8		608.8	608.4	2-(1,1'-biphenyl-4-y)-N-(1S)-2-(1-metnyl-1H-indol-3-y)-1- ((metnyl(1S)-2-(metnylamino)-1-(2- naphitnylmethyl)etnyljamino)metnyl)etnyljacetamide	8:	u	N	N
Boc-L-(2-Naphthyt)-alanine Boc-L-(2-Naphthyt)-alanine 4-Ethyt-4-Biphenylcarboxylic acid Boc-L-(2-Naphthyt)-alanine Boc-L-(2-Naphthyt)-	23	[Boc-L-(2-Naphthyt)-alanine][Boc-L-(2-Naphthyt)-alanine][Boc-L-(2-Naphthyt)-alanine]	541.7	541.3	N-{(1S)-2-{metryl(1S)-2-(metrylamino)-1-(2- naphtrylmetryl)atrylamino)-1-(2-naphtrylmetryl)atryl]-4- vinylbenzamide	8. 8.	4		~
(Boc-L-(2-Naphthyl)-alanine)[Boc-L-(2-Naphthyl)-alanine)[3.5-Bis-(trifluoromethyl)-phenylacetic acid	. 2	[Boc-L-(2-Naphthyl)-alanine][Boc-L-(2-Naphthyl)-alanine][4-Ethyl-4-Biphenytcarboxylic acid]	619.9	619.4	4*ettyl-N-[(15)-2-(metryl[(15)-2-(metrylamino)-1-(2- naphthylmetryl)ethyljamino)-1-(2-naphthylmetryl)ethyl]-1,1'- biphenyl-4-carboxamide	\$3 9 0	4	2	N
	33	(Boc-L-(2-Naphthyl)-alanine][Boc-L-(2-Naphthyl)-alanine][3 5-Bis-(trifluoromethyl)-phenylacetic acid	665.7	665.3	2-[3,5-bis(trifluoromethyl)phenyl]-N-[(1S)-2-{methyl(1S)-2- (methylamino)-1-(2-nephthylmethyl)ethylamino)-1-(2- naphthylmethyl)ethyllacetamide	6.9	4	٥ .	7
591.8 591.3	42		. 591.8	591.3	N-[(15)-2-(methyl[(15)-2-(methylamino)-1-(2- naphthylmethyl)athyllamino]-1-(2-naphthylmethyl)athyl]-1,1- biphenyl-4-carboxamide	6.2	4	2	. 2

	TPI1349 Studius Figure 21	MW	Evact Mass	***	0		9		
	Soci-(2-Naphthyl)-atanine Boct_(2-Naphthyl)-atanine Boct_(2-Naphthyl)-atanine Boct_(3-Naphthyl)-atanine 4-8 phenylacetic acid		605.3	abyl(15)-2-(methylamino)- hylamino)-1-(2- filacetamide	M. 19	HBONDACCEPTON KUIBUITIVE 4 2 2 2	2	Cule Cirios	
26 [Box	Boc-L-(2-Naphithyl)-alanina Boc-D-Tryptophan 4-Vmytbenzoic acid	544.7	544.3	W-[(1R)-2-(1-methyl-1H-indol-3-yl)-1-((methyl(1S)-2- (methylamino)-1-(2-naphthylmethylethyllamino)methyl)ethyl)- 4-vinylbenzamide	. 8.3	v	2	2	
27	Boc-L-(2-Naphthyl)-planina Boc-D-Typtophan 4-Etry4-4-Biphanylcarboxylic acid	622.9	622.4	4-ethyt-N-{(1R)-2-{1-methyl-1H-indol-3-yl)-1-{(methyl[1S)-2. (methylamino)-1-{2-methylminolmethyl]ethyl-5 (methylamino)-1-{2-methylmethylethylethylethyl-5 (methylaminolmethyl)ethyl-5 (methylaminolmethyl)-1-2-phenyl-4-carboxamide	5.2	v		2	
28	Cra Cra Craptity) - elanina Boc. D. Tryplophan 3,5-Bis-(lifiluoromethyl)-phenylacetic acid	668.7	668.3	2-{3,5-bis(trifluoromethyl)phenyl-l-l-{1R}-2-(1-methyl-1H-indol 3-yl)-1-{(methyl(1S)-2-(methylamino)-1-{2- naphthylmethyl)ethyljamino)methyl)ethyljacetamide	80 15	vs	N	۸	
29	Boc-L-(2-Maphihyl)-alanina)[Boc-D-Typtiophan][4-Biphenytcarboxylic acid]	594.8	594.3	N-[(1R)-2-(1-methyl-1H-indol-3-yl)-1-((methyl((1S)-2- (methylamino)-1-(2-naphhylmethyl)ethyljamino)methyl)ethyl]- 1,1'-biphenyl-4-carboxamide	d. Où	va ´	8	8	_
30	Boc-L-(2-Naphthyt)-elanine Boc-D-Tryptophan [4-Biphenylacatic acid]	608.8	608.4	2-(1,1'-bipheny/-4-y)-N-((1R)-2-(1-methyr-1H-indol-3-yl)-1- ((methyll(1S)-2-(methylamino)-1-(2- naphthylmethyljethyljamino)methyl)ethyljacetamide	4. Ø.	u	2	2	
Pi1349 Structures	ctures				\dagger				

TP11349	TPI1349 Structures FIGURE 21	WW	Exact Macs	omoN	1	**		
٤	Boc-L-Leucine][Boc-D-Tryptophan][Acetic acid]	372.6	372.3	Name N-{(1R)-2-(1-methyl-1H-indol-3-yl)-1-{(methyl(1S)-3-methyl-1- ((methylamino)methyl)autyl)anino)methyljathyl)acetamide	AL09P	HBondAcceptor	HBondDonor 2	Rule Offive 0
TP11349	TPI1349 Structures							
33	Cos Cost Cost Cost Cost Cost Cost Cost C	531.6	531.3	C. N-{(15)-1-benzy-2-(methyl{(15)-3-methyl-1- [(methylamino)athyl)-2-13.5- bis(trifluoromethyl)phenyl]acetamide	S Si	4	8	2
33	Boc-L-Leucine) Boc-L-Phenylalanine 4-Vinylbenzoic acid	407.6	407.3	N-[(1S)-1-benzyl-2-(metryl(1S)-3-metryl-1- ((metrylamino)metryl)butyl)amino)etryl}-4-vinylbenzamide	4. t.	4	2	۰
8		485.7	485.3	v N-[(1S)-1-benzyt-2-(methyl((1S)-3-methyl-1- [(methylamino)methyl]buyl)amino)ethyl-4-ethyl-1,1'-biphenyl- 4-carboxamide	5.1	4	8	-

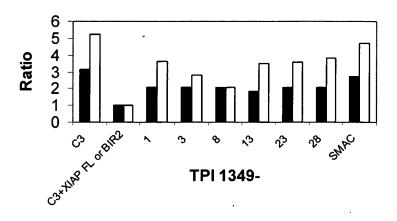




TPI 1349

Figure 21B

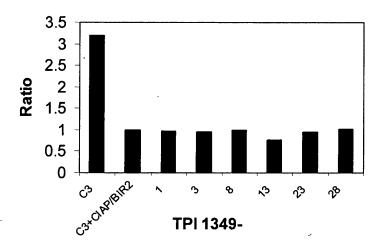
Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058 34/123



■ XIAP-FL □ XIAP-BIR2

FIGURE 21C

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058 35/123



 $100 \mu g/ml \ 10, \ 2003$

FIGURE 21D

TP11396	CHÉMISTRY FIGURE 22	MW	Exact Mass	Name	MLogP	HBondAcceptor	IHBonnOppor	RuleOfFive
1	(Bac-O-Lysine(2-Ci-Z-Lysine(a-Bac)) 4-Methosypnenylacetic acid	1003.3	1002.5	N-{(5R)-6-{(anilinocarbonyl)amino}-5-((anilinocarbonyl){(2S) 6-{(anilinocarbonyl){2-{4-methoxyphenyl)ethyljamino}-2- {(anilinocarbonyl){methyljamino}hexyljamino}hexylj-N- methyl-N-phenylurea		16	đ	4
2	(Boc-O-Lysine(2-Ci-2)[3-Ci2-L-Lysine(e-Boc)[1-Adamantaneacetic acid]	1031.4	1030.e	N-[2-[1-adamanty ethyl]-N-[(5S)-8-[(anilinocarbonyi)((1R)-1 ((fanilinocarbonyi)amino methyl)-5- ((anilinocarbonyi)(methyl)amino pentyl]amino -5- ((anilinocarbonyi)(methyl)amino hexyl)-N-phenylurea	5,1	15	đ	4
3	(Boc-O-Lysine(2-C)-Z)/[B-C/Z-L-Lysine(4-Boc))[Cyclohexanebutyric acid]	1007.3	1006.5	N-{(SR)-6-{(anilinocarbonyl)amino}-5-((anilinocarbonyl){(2S)-8-{(anilinocarbonyl){(2S)-8-{(anilinocarbonyl){4-cyclohexylbutyl)amino}-2-{(anilinocarbonyl){methyl)amino}hexylyamino)hexylyn-N-methyl-N-phenylurea	4.8	15	6 _	4
4	[Boc-O-Lysine(2-C-b-Z)][Boc-L-Norleuche][4-Methoxyphenylacetic actor]	855.1	854.5	N-{(SR)-6-{(anilinocarbonyl)amino}-5-{(anilinocarbonyl)(2S}- 2-{(anilinocarbonyl)(2-(4- methoxyphenyl)ethyljamino)hexyl)amino)hexyl}-N-methyl-N'- phenylurea	4.5	13	. 5	3
5	/Boc-Q-Lysinet2-CI-Z)//Boc-L-Norisucine / 1-Adamantanescetic acid	583.2	882. G	N-[2-(1-adamanty)]ethy]-N-((1S)-1-{((anilinocarbonyl))((1R)- 1(((anilinocarbony)]amino[methyl)-5- ((anilinocarbony))(methyl]amino[pentyl]amino]methyl[pentyl] N°-phenylurea	5.5	12	5	3
đ	[Boc-D-Lysine(2-Cl-Z)]Boc-L-Norseycine (Cyclohexanebutyric acid]	859.2	858.6	N-{(SR}-6-{(anilinocarbonyl)amino -5-{(anilinocarbonyl)}{(2S)- 2-{(anilinocarbony)/4- cyclonexylbutyl)amino hexylj-N-methyl-N- phenylurea	5.2	12	5	3
7	[Boc-O-Lysine (2-C)-Z)[Boc-O-Phenylalanine][4-Methoxyphenylacetic acid]	889.1	888.S	N-{(5R)-9-{(anilinocarbonyl)amino}-5-{(anilinocarbonyl)((2R)- 2-{(anilinocarbonyl)(2,4-methoxyphanyl)athyljamino}-3- phenylpropyl)amino}hexyl}-N-methyl-N'-phenylurea	4.8	. 13	5	3
a	[Boc-O-Lysine/2-CI-ZI/Boc-O-Phenyyalanine (1-Adamantaneacetic gcid)]	917.2	918.5	N-12-(1-adamantyl)ethyl-N-((1R)-2-((anilinocarbonyl)((1R)-1 (((anilinocarbonylamino)methyli-S- ((anilinocarbonyl(methyl)amino)jantylyjamino)-1- benzylethyl -N'-phenylurea	5.8	12	5	3

TP11398	CHEMISTRY FIGURE 22	MW	Exact Mass	Name	MLogP	HBondAcceptor	HBondOoner	RuteOfFive
, g	[Boc-D-Lysine/2-Cl-Z)]Boc-D-Phenylalanine Cyclohexanebutyric acid	893.2	892,5	N-{(\$R)-6-{(anilinocarbonyl)amino}-5-{(anilinocarbonyl){(2R) 2-{(anilinocarbonyl){4-cyclohazylbutyl)amino}-3- phenylpropyl)amino hexyl}-N-methyl-N-phenylurea	5.5	-12	5	3
10	(Boc-O-Lysinet2-CI-Z)[Boc-L-Profine] 4-Methoxyphanylacetic acid1	719.9	719.4	N-((5R)-6-((anilinocarbony))amino -5- {(anilinocarbony)(((2S)-1-(2-4- methoxypheny))ethyllpyrrolldin-2-yi[-nethyl)amino hexy[-N- methyl-N-phenylurea	3.7	11	4	2
- 11	(Boc-D-Lysine(2-Ci-Z)[Boc-L-Proline [1-Adamantanescetic acid]	748.Q	747.5	N-(((2S)-1-{2-{1-adamanty/)ethylpyrrolidin-2-y/kmethyl}-N- ((1R)-1-(((anilinocarbonyl)amino methyl}-S- ((anilinocarbonyl)(methyl)amino pentyl}-N-phenyturea	4.9	10	4	2
12	[Boc-D-Lysine(2-Cl-Z))Boc-L-Proline (Cyclohexanebutyric acid)	724.0	723.5	N-{(5R}-0-{(anilinocarbunyi)amino}-5-{(anilinocarbunyi){((2S) 1-(4-cyclohavylbulyi)pyrrolidin-2-yl methylamino)hexyl -N- methyl-N-phanyluraa	4.6	10	1	2
43	(Bac4_3-12-Naphthyl)-Alanins (a-CiZ4_4-ysine(e-Boc))(4-Methoxyphenylacetic acid)	939.2	938.5	N-{(1S}-2-{(anilinocarbony/)amino}-1-{2- naphthytmethylylethyl -N-{(2S}-0-{(anilinocarbony)}(2-{4- methoxyphenylylethyljamino}-2- {(anilinocarbony/)(methyljamino)hexyl}-N-phenyluraa	5,2	. 13	5	. 3
14	[Boc-L-3-(2-Naphthyl)-Alanine [a-C/2-1-1/sine(a-Boc)[1-Adamantaneacetic acid]	987.3	966.đ	N-[2-{1-adamantyl)ethyl]-N-((5S)-6-{{anilinocarbonyl} [1S}-2 ({anilinocarbonyl)amino}-1-{2-naphthylmethyl)ethyljamino}-5 ({anilinocarbonyl)(methyl)amino hexyl]-N'-phanyturea	6.2	12	S	3 .
15		943.2	942.6	N-{{18}-2-{{anillnocarbonyi}amino}-1-{2- naphthy/methyllethyl-N-{(2S)-4-{anillnocarbonyi}{4- cyclanaxylouryi}amino}-2- {{anillnocarbonyi}{methyi}amino hexyi}-N'-phenyturea	5.9	12	S	3
. 15	(Boct-3-12-Nagnthyl)-Alanine (Facet -Nagnthyl)-Alanine (Facet -Nagnthy	791.0	790.4	N-{(1S}-2-{(anifinocarbony))amino}-1-(2- naprithymethyl)athyl-N-((2S)-2-{(anifinocarbony))2-(4- methoxypneny)ethyl]amino}hexyl}-N'-phenyiurea	5.6	10	4	2
	FIG	JUR	E 22Å	(cont.)		— — — L		لـــــــ

Title: METHODS AND COMPOSITIONS FOR...

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TP11398	CHEMISTRY FIGURE 22	MW	Exact Mass	Name	MLogP	HBondAcceptor	HBandDanar	RuleOfFiv
. 17	[Boc.1-3-(2-Naphtnyl)-Alanine [Boc.1-Norleucine [1-Adamantanescetic acid]	819,1	818.5	N-{2-{1-adamanty/)ethyi -N-{{1:3}-1-{{(anilinocarbonyi){{1:5}-2-{(anilinocarbonyi)}{1:5}-1-{2-naphthyimethyi)ethyi aminojmethyi)pantyi -N-phenyiurea	6.3	9	4	2
18	[Boct_3-(2-Naonthyl)-Alanine [Boc-L-Norleucine](Cyclohexenebutyric acid)	795.1	794.S	N-{(18)-2-{(aniilnocarbonyt)amino}-1-{2- naphthyimethylyathyl-N-{(25)-2-{(aniilnocarbony);(4- cyclohexylbutyl)amino hexylj-N*-phenylures	6.0	g	4	2
19	[Boc-L-3-(2-Naghthyl)-Alanine [Boc-Q-Phenylalanine [4-Methoxyphanylacetic acid]	825.0	624.4	N-{(1S)-2-{(enilinocarbonyl)amino}-1-{2- naphthylmethyl)ethyl-N-{(2S)-2-{(anilinocarbonyl)2-{4- methoxyphenyl)ethyljamino}-3-phenylpropyl)-N-phenylurea	. 5.9		4	2
20	[Boc-1-3-12-Naphthyl)-Alanine (Boc-0-Phenylalanine) 1-Adamantaneacetic acid)	853.1	852.5	N-{2-{1-adamantyl)ethyl -N-{(1S)-2-{(aniilnocarbonyl){(aniino})-1}}}}}}}}}	5.6	9	•	2
21	[Boc4-3-(2-Naphthy)-Alanine (Boc-0-Phenvialanine) (Cyclohexanebutyric acid)	829.1	528.5	N-{{1S}-2-{{anilinocarbonyl}amino}-1-{2- naphthylmethyl)ethyll-N-{{2S}-2-{{anilinocarbonyl}(4- cyclohexylbulyl)amino}-3-pnenylpropyl)-N-phenyluraa	8.3	· 9	•	2
22	IBac-L-3-(2-Naphthyl)-Alanine Boc-L-Proline 4-Methoxyphenviacetic acid	655,8	655.4	N-{{1S}-2-{{aniifinocarbony }amino -1-{2- napnthymethy }ethy -N-{{(ZS}-1-{2-4- methoxypheny }ethy pyrrolidin-2-yf}methy }-Y-phenylurea	4,6	8	3	2
23	(Boct-3/(2-Naghthyl)-Alanine (Boct-Proint) 1-Adamantaneacetic acid)	683.9	583.4	N-(((2S)-1-(2-(1-adamantyl)ethyl)pyrroidin-2-yi)methyl)-N- ((1S)-2-((anilinocarponyl)amino)-1-(2-naphthylmethyl)ethyl)- N-phenylurea	5.8	7	3	2
24		đ59.9	đ59.4	N-{(1S}-2-{(anilinocaroonyl)arnino}-1-{2- napnthymethyl)ethyl-N-{[(2S}-1-4- cyclonexytburyl)pyrrolidb-2-yr]methyl-N-phanylurea	5.4	7	3	2

FIGURE 22A (cont.)

Title: METHODS AND COMPOSITIONS FOR... Inventors: Reed et al.

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Docket No.: 66821-058

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TP11396	CHEMISTRY FIGURE 22	MW	Exact Mass	Name	MLogP	HBandAcceptor	HBondDonar	RuteOfFive
25	[Boc-D-Cyclohexyletanine] a-ClZ-L-Lysing(e-Boc)] 4-Methoxypnenylacetic acid]	895.2	· 894.5	N-{(1R)-2-{(anilinocarbonyi)amino}-1- (cyclohexyimethy)leh(/(2S)-6-((aniinocarbonyi){2-{4- methoxyheny)lehylamino; (anilinocarbonyi)(methyi)aminofitexyi)-N-phanyiurea	4.6	13	5	3
25	(Boc-0-Cyclohaxytalanine te-CiZ-L-Lysine(e-Boc)) 1-Adamanteneacetic acid	923.3	922.6	N-{2-{1-adamentyl)ethyl-N-{(\$\$)-8-{(anilinocarbonyl)((18)- ([arilinocarbonyl)amino)-1-{-cyclohexylmethyl)ethylamino)-1 ((anilinocarbonyl)(methyl)amino hexyl)-N-phenylurea	8.0	12	5	3
27	[Boc-O-Cyclohexytstanine] a-CiZ-L-Lysine(e-Boc))Cyclohexanebutyric acid)	899.2	394.3	N-{{1R}-2-{{aniilnocarbonyl}amino}-1- (cyclohexylmethyl)ethyl-N-{{12S}-3-{{aniilnocarbonyl}{4- cyclohexylbutyl}amino}-2- {{aniilnocarbonyl}(methyl)amino}hexyl -N'-phenylurea	5.7	12	5	3
28	[Boc-Q-Cyclohexytalanine [Boc-L-Norleucine]] 4-Methoxyphenylacetic acid]	747.0	746.5	N-{{1R}-2-{{anifinocarbonyl}eminc}-1- (cycloherylmethyl)ethyl-N-{(25)-2-{(anifinocarbonyl)2-{4- methoxyphenyl}ethyl]amino}hexyl}-N-phenylurea	4.9	10	4	2
29	[Boc-O-Cyclohexylalanine][Boc-1Norleucine][1-Adamantaneacetic acid]	775.1	774.5	N-{2-{1-adamanty }ethyl}-N-{(1S)-1-{((anilinocarbonyl){(1R)-2 ({anilinocarbonyl){(1R)-2 ({anilinocarbonyl)}-nnino}-1-(cyclohexylmethyl)ethyl amino}-methyl)pentyl]-N'-phenylurea	6.1	9	4	2
30	(Boc-Q-Cyclohexytalenine (Boc-1-Norteucine (Cyclonéxerieputyric acid)	751.1	750.5	N-{(1R)-2-{(anilinocarbonyl)amino -1- (cyclohaxyimathyl)athyl -1-((2S)-2-{(anilinocarbonyl)(4- cyclohaxyibutyl)amino haxyl -N'-phenyturaa	5.8	9	4	2
31	[Boc-Q-Cyclohexylalanine [Boc-Q-Phenvialanine [4-Methoxyphenviacetic acid]	781.0	780.4	N-{{ : IR}-2-{{anilinocarbony }amino}-1 - (cyclohaxytinethyl)ethyl}-N-{(2R)-2-{{anilinocarbonyl}(2-{4- methoxyphenyl)ethyl amino}-3-onenylpropyl}-N-phenylures	5.2	10	4	2
12	[Boc-O-Cyclohexvistanine] Boc-QPhenvisianine] 1-Adarmantaneacetic acid]	809.1	908.5	N-[2-(1-edamantyl)ethyl]-N-[(1R)-2-((anilinocarbonyl)((1R)-2 (anilinocarbonyl)aminoj-1-(-cyclohexylmethyl)ethylaminoj-1- benzylethyl)-N*-phenylurea	6.4	9	4	2

FIGURE 22A (cont.)

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TP1:396	CHEMISTRY FIGURE 22	MW	Exact Mass	Name	MLogP	HBondAcceptor	HBangDoner	RuleOfFive
33	(Boc-D-Cyclohexytalanine#Boc-D-Pnenytalanine#Cyclohexanebutyric acid]	785,1	784.5	N-{{1R}-2-{{anilinocarbonyl}amino}-1- (cyclohesylmethyl)ethyl-N-{(2R}-2-{{anilinocarbonyl}{4- cyclohesylbutyl)amino}-3-phenylpropyl}-N-phenylurea	6.0	9	4	z
34	[Boc-O-Cyclonexytalanine [Boc-4-Proline] 4-Methoxypnenylacetic acid]	511.8	611.4	N-{{1R}-2-{{anilinocarbonyl}amino}-1- (cyclohaxylmethyl)ethyl}-N-{{(2S}-1-{2-{4- methoxyphenyl)ethyl]pyrrolldin-2-yl}-methyl)-N'-phenylurea	4.3	8	3	2
35	(Soc-O-Cyclohexylatanine)[Boc-IProline][1-Adamantanescetic acid]	639.9	639. 5	N-{((23)-1-{2-{1-adamanty/jethy/[pyrrolidin-2-yi]:methyl]-N- {(1R)-2-{(anliinocarbonyljarring-1-(cyclohexylmethyl)ethylj- N-phenylures	5.5	7	3-	. 2
38	[Boc-Q-Cyclohexylatanine] Boo-L-Proline] Cyclohexanebutyric acid]	615.9	615.5	N-[(1R)-2-[(anilhocarbony/)amino]-1- (cyctohaxylmethyl)-thyl-N-[[(2S)-1-14- cyctohaxylbutyl)pyrroldin-2-yl]methyl-N-phenylurea	5. †	7	3	2
37	CHEMISTRY CHEMISTRY (Boc-L-Phenytalanine [Boc-L-Phenytalanine [1-Phenyt-1-Cycloproganecarboxylic acid]	771.0	770.4	N-((1S)-2-{(aniiinocarbonyi)amino -1-benzytethyf -N-((2S)-2- ((aniiinocarbonyi)(1-phenyicyclopropyjmethyljamino -3- phenyipropyi)-N-phenyiursa	5.7	9	•	2
38	[Boc-L-Phenyslanines[Boc-L-Phenyslanines[b-ToMacetic scid]	759.0	758.4	N-{{1S}-2-{{aniiinocarbonyl}amino}-1-benzylethyl}-N-{(2S}-2- {{aniiinocarbonyl}2-{4-methylphenyl}ethyljamino}-3- phenylpropyl}-N-phenyluree	5.9	9 .	4	2
19	[Boc-L-Phenylalanine [Boc-L-Phenylalanine [3-Methoxypnenylacetic acid]]	775.0	774,4	N-{ 1\$}-2-{ aniilnocarbony amino -1-benzylethy }-N-{(2\$}-2- (aniinocarbony)2-{3-methoxypheny }ethy]amino}-3- phenylpropyl)-N-phenylurea	5.4	10		2

FIGURE 22A (cont.)

TPI1396	CHEMISTRY FIGURE 22	MW	Exact Mass	Name	MLogP	HBondAcceptor	НВпопОсе-	1911-0-
41	(BoctPhenylalanine [BoctPhenylalanine [4-Ethoxyphenylacetic acid]	789.0	788.4	N-{{1S}-2-{{anilinocarbonyl}aminoj-1-benzylethyl}-N-{{2S}-2- {{anilinocarbonyl}2-(4-ethoxybnenyl)ethyl]aminoj-3- phenylpropyl}-N-phenylurea		10	4	- Z
42	(Bac-L-Phenylalanine (Bac-L-Phenylalanine (Phenylacenc scid)	744.9	744,4	N-{(15)-2-{(aniilnocarbonyl)amino -1-benzylethyl}-N-{(25)-2- {(aniilnocarbonyl)(2-phenylethyl)amino -3-phenylpropyl}-N- phenylurea	5.7	9	4	2
43	[Boc-L-Phenylalanine] Boc-L-Phenylalanine] Hydrocinnamic acid]	759.0	758.4	N{(1S)-2-{(anilinocarbony/)amino -1-benzylethyl)-N{(2S)-2- ((anilinocarbonyl)(3-phenylpropyl)amino -3-phenylpropyl)-N- phenylurea	- 5.9	9	•	2.
	[Boc-L-Phenylalanine [Boc-L-Phenylalanine [Burvinc acid]]	696,9	696,4	N-((15)-2-{(ariilinocarbonyi)a.mino -1-benzylethyi}-N-((25)-2- ((aniilinocarbonyi)(butyi)amino -3-phenylpropyi]-N'- phenylurea	5.3	g	4	2
45	[Boc_L-Phenylalanine [Boc_L-Phenylalanine [Heptanoic acid]	739.C	738,4	N-{(1S}-2-{(anilinocarbonyi)amino}-1-benzyethyi}-N-{(2S}-2- {(anilinocarbonyi)(heptyi)amino}-3-phenyipropyi}-N- phenyturea	5.8	9	4	2
45	(Boc-L-Phenylalanine (Boc-L-Phenylalanine (Isobutyric scid)	896.9		H(18)-2-{(anifinocarbony) amino -1-benzylethy -N-(128)-2- (anilinocarbony) aoouty amino -3-chenylpropy -N- chenylurea	5.3	. 9	4	2
47 !		724.9	724.4 [(2	-{{ 1S}-2-{{ anilinocarbonyl}amino}-1-benzylethyl}-N-{{ 2S}-2- Inilinocarbonyl}4-methylpentyljamino}-3-phenylpropyl}-N- phenytursa	5.6	9	4	
48		710.9	710.4 N-1	(13)-2-((aniilmocarbonyt)amino -1-benzyriethyf)-N-((25)-2- (andinocarbonyt)(neopentyt)amino -3-pnenytyropyt)-N- phenyturea	5,4	g	4	2

TPI1396	CHEMISTRY FIGURE 22	MW	Exact Mass	Name	MLogP	HBondAcceptor	HBandOanar	RuleOfFive
49	[Boc-L-Phenylalanine (Boc-L-Phenylalanine) [Flort-Burylacetic acid]	724.9	724.4	N-{(1S)-2-{(enillnocarbonyl)amino -1-benzylethyl}-N-{(2S)-2- {(anilmocarbonyl)(3.3-dimethylburyl)amino -3-pnenylpropyl}- Nr-phenyturea		9	4	2
50	[Boc-L-Phenylsianine [Boc-L-Phenylsianine [Cyclohexanecarboxylic acid]]	737.0	736.4	N-{(1S}-2-{(aniilnocarbonyl)amino}-1-benzylethyl}-N-{(2S}-2-{(aniilnocarbonyl)(cyclohexylmethyl)amino}-3-phenylpropyl}- N-phenylures	5.4	.g	4	2
51	(Boc.LPhenylatanine [Boc.LPhenylatanine [Cyciohexylacetic acid]	751.0	750.4	N{(1S}-2-{{aniiinocarbonyi}amino}-1-benzy/ethyl}-N{(2S}-2- [{aniiinocarbonyi}{2-cyclohexylethyljamino}-3-phenylpropyl}- N-phenylurea	5.5	9	4	2
52	[Boc.tPhenylalanne [Boc.4-Phenylalanine] Cyclohexanebutync acid]	 779.0	778.5	N-{{1S}-2-{{aniiinocaroonyi}amino}-!-benzylethyf}-N-{{2S}-2- {{aniiinocarbonyi {4-cyclohexylbubyljamino}-3-phenylpropyl}- N'-phenylurea	5.8	9		2
53	[Boc-t-Phenytalanine]Boc-t-Phenytalanine]Cycloheptanecarboxytic acid]	751,0	750.4	N-{{ 1S}-2-{{ aniiinocarbonyi}amino}-t-benzytethyt}-N-{{2S}-2- ({aniiinocaroonyi}(cycloheptylmethyl)amino}-3-phenylpropyt} N-phenylurea	5.5	9	4	2
54	[Boc-L-Phenyislanner [Boc-L-Phenyislanine [Acaba said]	668.8	668.3	N-{{1\$}-2-{{anilinocarbony amino -1-benzylethyl-N-{(28}-2- (anilinocarbony (ethyl) amino -3-phenylpropyl -N- phenylurea	4.9	9	4	2
55	/Boc-L-Phenylaisnine [Boo-L-Phenylaisnine [Cyclobutanecarboxylic acid]	708.9	708.4	N-((13)-2-{(anilinocarbonyi)amino -1-benzyrethyi)-N-((25)-2- ((anilinocarbonyi)(cyclobulymethyi)amino -3-phenyipropyi)- N-phenyiurea	5.0	9	•	2
56	(Bool,-Phenylstanine) Bool,-Phenylstanine) Cyclopentanecarpoxylic acid	722.9	722.4	v-{(13}-2-{(aniänocarbonyi)arrino}-t-benzyisthyi}-N{(25}-2- (aniänocarbonyi}(cyclopentyimethyi)amino}-3-phenyipropyi} N*-phenyturea	5.2	. g [.]	4	7

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TPI1396	CHEMISTRY FIGURE 22	MW	Exact Mass	Name	MLogP	HBandAcceptar	HBandDonor	RuteOfFive
57	/Boc-t-Phenylalanine Boc-t-Phenylalanine Cyclohexanepropionic acid	765.0	784,4	N-{(1S}-2-{(anilinocartonyl)amino -1-benzylethyl}-N-{(2S}-2- {(anilinocartonyl)(3-cyclohexylpropyl)amino -3- phenylpropyl}-N-phenylurea	5.7	9	4	ż
58	[Boc-L-Phenylalanine [Boc-L-Phenylalanine [4-Metryl-1-cyclonexanecarboxylic acid]	751.0	750.4	N-{(1S)-2-{(aniinocarbonyi)amino}-1-benzylethyi}-N-{(2S}-2- ((aniinocarbonyi)(4-methyicyclohexyi)methyi jarmno}-3- phenyipropyi}-N-phenylurea	5.5	9	4	2
Sa ´·	[Boc-L-Phenylalanine Boc-L-Phenylalanine 4-tent-Butyl-cycloheranecarboxylic acid	793.1	792.5	N-{{15}-2-{{anilinocarbonyl}amino}-1-benzylethyl}-N-{{25}-2- {{anilinocarbonyl}{(4-tent-butylcycishexyl)methyl amino}-3- phenylpropyl-N-phenylurea	6. 0	9	•	2
60	[Boc-L-Phenylalanine §Boc-L-Phenylalanine § (-Adamantaneacetic acid)	803.1	a02.5	N-[2-{1-adamanty/)ethylj-N-{(1S)-2-{(aniiinocarbonyi){(1S)-2- ((aniinocarbonyi)aminoj-1-benzylethyljaminoj-1- benzylethylj-N-phenyturea	6.2	9 .	4	2
d 1	(Boc.1-Phenytalanine (Boc.1-Phenytalanine (3,3-O)phenytpropionic acid)	835.1	834.4	N-(1S)-2-(aniilnocarbony) amino -1-benzylethyl)-N-(2S)-2- [(aniilnocarbonyl)(3,3-diphenylpropyl)amino -3- phenylpropyl-N-phenyluraa	5.6	9 _	•	2
62		737.0	735.4	N-{{15}-2-{{aniänocarbonyi}amino -i-benzylethyl}-N-{{25}-2- {{aniinocarbonyi}{2-cyclopentylethyl}amino -3-phemylpropyi} N-phenyturas	5.4	9	4	2
63	[BootPhenylalanine] BootPhenylalanine] Cyclopentylacetic acid]	784.0	783.4	N-{(15}-2-{(snilinocarbonyi)smino}-1-benzylethyi}-N-{(25}-2- ((anilinocarbonyi)[2-{11-indol-3-yi)ethyi]amino}-3- phemypropyi]-N-phenylurea	4.5	10	5	2
84	(Boot-Phenylalanina [Boot-Phenylalanina [3-(3.4, 5)-Trimethoxyphenylpropionic actor)	849.0	348.4	+-((15)-2-{(anilinocarbonyl)amino}-t-benzylethyl}-N-((25)-2- (anilinocarbony)(3-4).4.5-trimethoxypnemyl)propyl]amino}-3 phenylpropyl)-N-phenyturea	4.5	12	4	1

TPI1396	CHEMISTRY FIGURE 22	MW	Exact Mass	Name	MLogP	HBandAcceptor	HBandDanar	RuleOfFive
85	[Boc-L-Phenyisianine [Boc-L-Phenyisianine [Z-Norbornanescritc scid]	783.0	782.4	N-{{1S}-2-{{anilinocarbonyl}emino}-1-benzylethyl}-N-{{2S}-2- {{anilinocarbonyl}?-bicyclo[2.2.1]hept-2-ylethyl}emino}-3- phenylpropyl}-N-phenylurea		9	4	2

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058

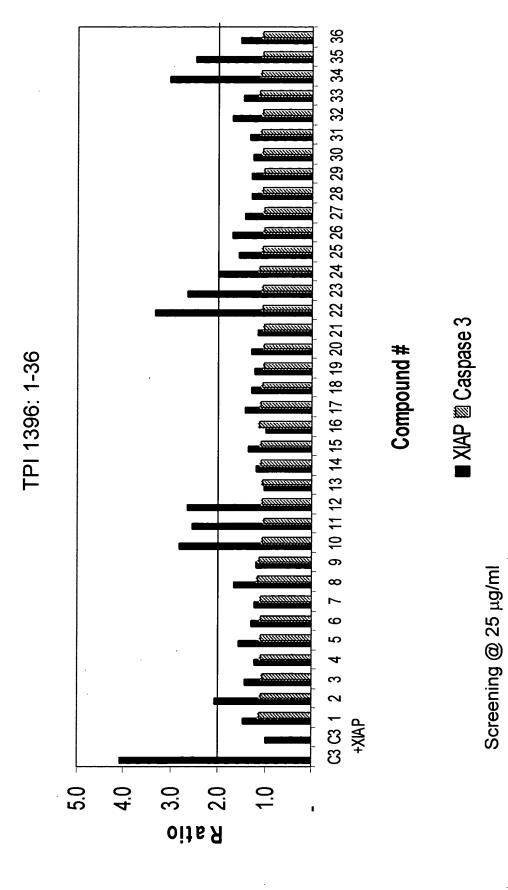
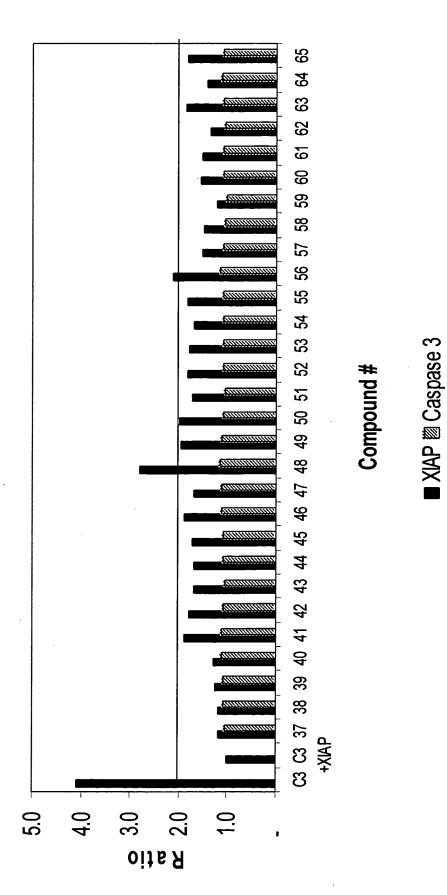


FIGURE 22B

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TPI 1396: 37-65



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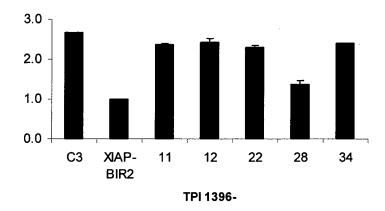
FIGURE 22C

Selected TPI 1396

TPI 1396	Caspase 3- XIAP IC-50 (μΜ)	se 3-	Caspase 3-XIAP- BIR2 IC-50 (μM)	-XIAP-
	AVG	STD	AVG	STD
11	32.1	3.8	7.9	0.3
12	53.0	8.3	14.4	1.1
22	45.3	3.3	9.5	2.2
28	>134		134.1	0.3
34	77.1	11.0	13.6	0.9

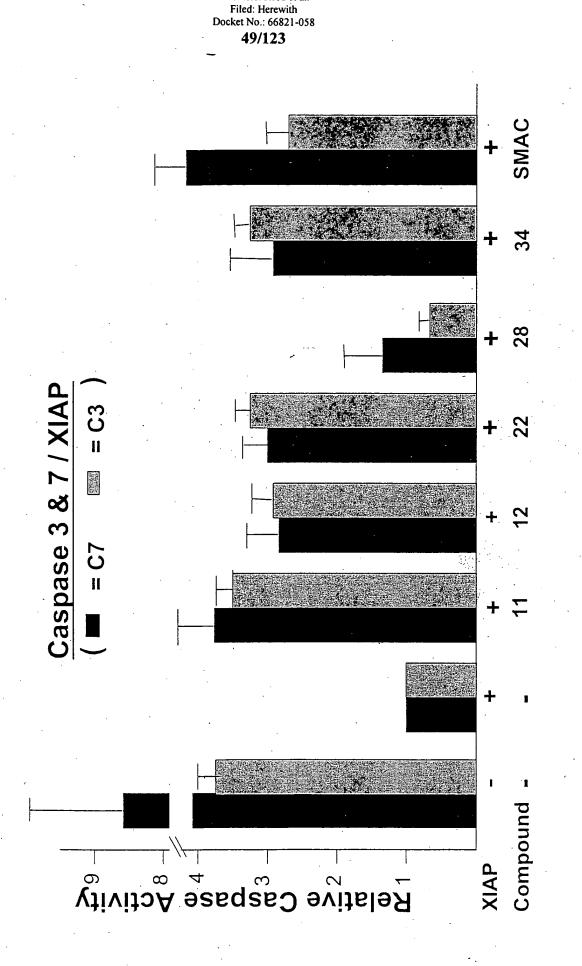
Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058

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 $50 \mu g/ml$ -Data 02,2003

FIGURE 22E



Title: METHODS AND COMPOSITIONS FOR... Inventors: Reed et al.

GURE 22F

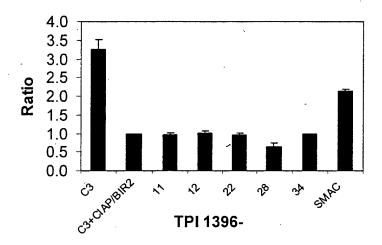


FIGURE 22G

TPI	391 Sinuctures Figure 23A	ww	Éxact Mas	s Name	MLogP			,
	[Fract. Noneucine [Frac.O.t. suche [4-1 sobusy-atoha-Mathylahenylacetis, Acti]	533.8	533,4	(SR)-1-((1 S)-1-((benzylanino)methylipemyl)-S-lackuy)4/2-(- iaobufylphenylipropylipperazina-2,3-done		, S	HBang Don	Or Rute OfFive
	CF3 CF3 Accord For Escal - New Chemistry	599.7	599.3	(5R)-1-((15)-1-((benzylambo)methylipentyl)-4-(2-(3,5- bis(trifluoromethyliphenyljethyl)-5-isobutylopenziche-2,1-dione	5.4	5		2
3	[FrocdNorteuchallFroc-Od-suchallPrestanois acid]	-457,7	457.4	(SR)-1-{(1-S}-1-{(Denzylamino)methyl(pentyl)-4-heptyl-5-leobuty(pipena) 2.3-dönna	3.7	s	1-	a.
	(Frace)_Norteucine()Frace-D-Leucine()(Alphe-Asphe-Asphe-Trift-ports-m-Toly() acertic solo()	\$31.7	\$31,3	(SR)-1-((13)-1-((bencytamina)-metrylipantyl)-5-taobusyl-6-(243- (billuorometryliphanyl)adtyljapana zina-2,3-dona	44	5		. 2
5	IF moc.1. Horteuche Fmoc.0-1, excine 4-len-Busyl-cyclohessenecarbourte, solid	511.8	511.4	(SR)-1-((1S)-1-((benzylamino)methyl)penkyl)-6-((4-tert-bulyloydohezyl)methyl)-5-ksobulylolperzzine-2,3-done	4.5	5		
đ	IFmoc 4. Nortequire Fmoc -2-1_equire Tm_Tolylacetic acid	477.7	477,3	(SR)-1-((1S)-1-((beraytamino)methy()penty()-5-laobutyt-4-(2-(3- methy(pheny()ethy)(phenazine-2,3-done	7.9	5	1	a
7	[F mool_Nortexcite] [F mool_2.2-Nagnthy/signing (4-1-sock)/-eights -Methylonery/sockio Add)	d17.9	617.4 (5	SS-1-((15)-1-((berunterrino)methy)penny)-4-(2-(+isocuty)penny)propy(S-(2-raphthy)methy)piperazine-2,3-dione	5.4	, 5	1	2
a	FmoolNorteuche (Fmool-2-Naphthysianne 3.5-8ht Triburomethyli-Phemylaceto Acot	963.7	683.3 bis	(33)-1-((15)-1-(benzylamino)rosthyl)perkyl,-4-(2-(3,5- g(billuoromethyl)perkyl)-5-(2-rapritryzmethyl)pearazine-2,3-dione	8.2	5	1	2
9	Franci, Norleucznell Franci, 2 Nagnithylatanine (Heorenoic edd)	541.0	541,4	. (SS)-1-((1S)-1-((bercy:tamkre:intethyl)partyl)-4-heptyl-5-(2- napxthylmethyl)ploanz.zne-2,3-done	4.5	5	1	2

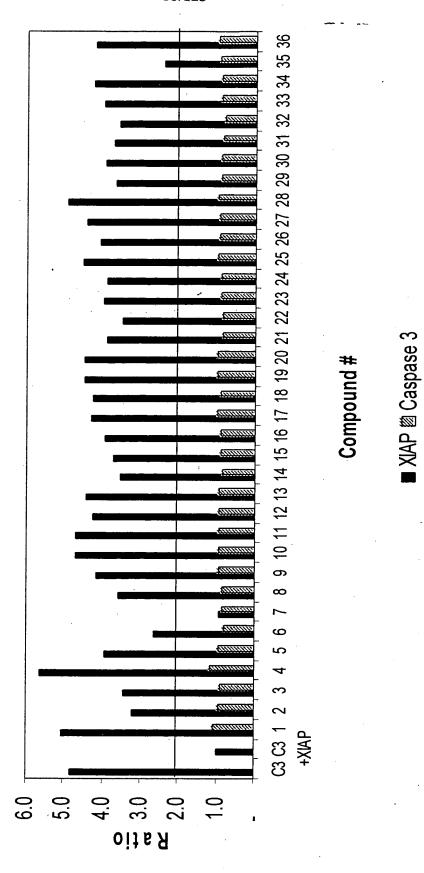
TP11391	Sinctures FIGURE 23A	MW	Exact Mass	s Name	MLogP	HBong Danor	HBondDonor	RuleOfFive
. 10	[Fmoc-L-Noteucine Fmoc-L-2-Naghtilly/latanine (Aloha-Alpha-Aloha-Triftacro-m-Tolvi) acatic acid	615.7	615.3	(SS)-1-((1S)-1-((benzylamino)-methylipennyl)-5-(2-naprithylmethyl)-6-(2-(3 (trifluoromethylipennyllethylippenapine-2,3-dione	5.3	5	1	2
11	Fmoc-t-Nortescine Fmoc-t-2-Naghthylainine 4-ter-Butyb-cycloheranecarboxylo-acid	595.9	595.4	(55)-1-((15)-1-((benzylamino)methylipentyl)-4-((4-lert- butylcyclohe ryl)methyl)-5-(2-napnthylmethyl)piperazine-2,3-done	\$3	5	1	2
12	IF moc.1. Northucina TF moc.1. 2. Naghthylasamne (m. Tohraceric social	561.5	561.3	(55)-1-{(15)-1-{(berzytarano)methylipenyi)-4-(2-(3-methyliphenyi)ethyl)-5 (2-naprithylmethyl)piparazine-2,3-dione	4.7	s	1	2
13.	(Free-Q-Norteacins & Free-Q-1, suches \$4-isotuty) -stoke-Aerthylphenylacetic Acid	\$33.6	533.4	(SR)-1-4(1R)-1-4(bencylamano)methylipentyl)-5-iaobutyl-6-[2-(4-iaobutyliphenyl)propylipiperazine-2,3-dione	4.5	5	1	2
14	IFmoc-0-Norleusins (Fmoc-0-Leucins ([3.5-8)() Trifupromethyl)-Phemylacatic Acid	599,7	599.3	(SR)-I-((1R)-I-(Denzyłamino)methylipentyl)-4-(2-(3.5- bis(trifluoromethyliphenyljethyl)-5-leobutylpiperazine-2,3-cione	5.4	5	t.,	2
15	IF moc-D-Norteucine F moc-D-Laucine Frephanos; acid	457.7	457,4	(SR)-1-((1R)-1-((bertrylamano)medhy(benhy)-4-hephyl-5-isobshybjeerszzne 2,3-done	3.7	S	t	
16	CP3 Frace-D-NorfeschreffFrace-D-Leucine [[Alpha-Alpha-Alpha-Trifluoro-n-Tolyr) acetic acid]	531.7	531.3	(5R)-1-((1R)-1-((benzylamino)metrylipentyl)-5-laobutyk-4-(2-(3- (trituorometryl)phenyljetryl)piperazine-2,3-done	4.4	5	1	2
17	From Q-hiofeuche (From Q-Leuche (4-tet-Butti-cyclohers necarposysto acid)	511.8	511.4	(SR)-1-((1R)-1-((bercy)ameno)methyl(penyl)-4-((4-tart- baylcyconexyl)methyl(-5-eopulytsiperszin-2,3-done	4.5	5	1	. 2
18	Frace-D-Morteructing (Frace-D-Leuctres (Im-Tolylacetic accid)	477.7	477.3	(SR)-1-((1R)-1-((bearzytamina imethyl)pentyl)-5-iaccusy-4-(2-(3- methylpnenyl)ethyl)pipenzzne-2,3-dome	3.9	·s	1	a

TPI	91 Structures FIGURE 21A	м	W Exact	Mass Name				
19	Froc-D-Norleucine (Froc-L-2-Naphthylatanine) A-laobuty-signa-Marimtohenylacetic Acid)				MLogP	HBendDonor	НВомаDane	RuleOffine
20	[Froc-Q-Norteucine] Froc -1 -2 Naphthy jalanine [3,5-3 ls/Trifluoromethy). Phanylacetic Acid!	583	7 663.:	(\$3)-1-{(1R)-1-{(Denzylamino)(nethyl)ponkyl)-4-(2-(3,5- ba((nfluoromethyl)phanyljethyl)-5-{(2-naphthylmethyl)piperazine-2,3-don	6.2	5		2
21	FALSE	541.	8 S41.4	(\$6)-1-{(1 R)-1-{(bency/actinins)/methylipentyl)-4-heptyl-5-{2- nsphitrykmethyl)japenrazine-2,3-dione	4.6	S	1	2
22	Fmoc-Q-Nortescine Fmoc4-2-Nagnthylatanine (Albria-Alpria-Alpria-Trifuora-m-Tolyn) scetic scid	615.7	615,3	(55)-1-{(1R)-1-{(bentzylamino)methyli)bentyl)-5-(2-naphthylmethyl)-6-(2-(3 (trifluoromethylipbenyl,lethylipbenzime-2,3-dione	5.3	5	,	2
23	[Frace-Q-Norleucine Frace-1-2-Nephthylatanine 4-lent-8-uny-cycloneranecarboxy/dc acid]	595.9	595.4	(\$\$)-1-{(1R)-1-{(ben'zyjamiro)methylipentyl}-4-{(4-ret- busylcyclonexyl)methyl-5-{2-raphthylinedhylipiperazire-2,3-dione	5.3	5	;	2
24	Fmoc-0-Norteucine (Fmoc-1-2-Negonitry)sawrine (m. Tolysacetic social	581.6	561,3	(53)-1-((1R)-1-((benzylannine)methyl[pentyl]-4-(2-(3-methylphenyl)ethyl]-5-(2-naphthylmethyl[piperazine-2,3-dlone	4.7	. 5	,	2 .
25	Fracc 4-2-Nephthylalanine (Fracc 3-Leucine (4-leobuty-alpha-Methylonenylacetic Ackd)	517.9	817.4	(SR)-1-(15)-2-(bentsyleneno)-1-(2-tashdrýmeltys)etnyl-3-laobutys-4-(2-(4-laobutyshenys)propys(laberacine-2,3-dione	5,4	5	1	2
25	moc-1-2-Naphthylatenne [Fmoc-2-Laucine (3.5-Bla(Trifluoromethyl)-Phenylacetic Actd]	583.7	583.3	(SR)-1-(15)-2-(benzylamero)-1-(2-rapitilylenedyr))edryl)-4-(2-(3,5-backithberomethyl)phenyl(edryl)-5-laobutylpherazzne-2,3-done	6.2	5	1	2
27	noc4-2-Ne onthvistanine (Fmos-O-Laucine (Heptanok; scid)	S41.8	541,4	(18)-1-(15)-2-(benzylamino)-1-(2-taghthylmethyl)ethylj-s-haptyl-5- isooutylpperazine-2,3-done	4.6		1	2

TPH 39	Sinuctures FIGURE 23A	MW	Exact Ma	ss Name	MLogP	I HBongOnov	H8andDonar	I 9 0
28	Fmoc-L-2-Naphthylaianine Fmoc-Q-Laucine (Alpha-Alpha-Alpha-Trifluoro-m-Tolyi) acetic acid	515.7	7 515.3	(5R)-1-{(15)-2-{bencylamino}-1-{2-raphthylmethyl)ethyl}-5-isobucyl-4-{2-{isobucyl-4-{isobucyl-4-{2-{isobucyl-4-{is	5.3	s		2
29	[Fmoc.1.2-Naphthylatanine]Fmoc.0-1.eucine \$4-ten-0.uhrl-cyclonezanecarboxysic social	595.9	\$95.4	(SR)-1-(18)-2-(benzylammo)-1-(2-naphthylmethyl)ethylj-4-(4-tart- bulyksycionaryl)methylj-5-laobusylajparazine-2,3-clione	5.3	5	1	2
30	IF moc-1-2-Na pritry istanine (Froc-D-1-sucine)(m. Tory iscense acid)	S61.8	561.3	(SR)-1-{(1S)-2-(benzylamino)-1-(2-nachthylmethyl)ethyl)-5-lacounyl-4-{2-(3 methylphenyl)ethyljpperazine-2,3-dicne	4.7	5	1	2
31	[Fmoc.\.2.44sprthylaterine (Fmoc.\.2.Naphthylaterine (Associaty-spins-Methylphenylacetic Acid)	702.0	701,4	(SS)-1-(15)-2-(benzylámmo)-1-(2-naphthylmethyl)ethyl)-4-(2-(4- isobutylphanyl)propyl)-S-(2-naphthylmethyl)piperazine-2,3-dione	5.2	5	1	2
32	[Froce1, 2-Maghtinylalanine] Froce1, 2-Maghtinylalanine (3,5-Bit) Trifluoromethyl)-Phenylacetic Acid]	767,8	757.3	(53)-1-((15)-2-(benzy)amino)-1-(2-taphthylmethyl)ethyl]-4-(2-(3,5-bis(trifloordmethyl)phenyljethyl)-5-(2-taphthylmethyl)piperazine-2,3-dione	7.0	s	1.,	2
33	Frace 1, 2-Maprimystanine (Frace 1, 2-Na prohysistenine (Fraptanoic acid)	625.9	625.4	(\$\$)-1-{(1\$)-2-(barczysarsino)-1-(2-rapphthylmethyl)ethyl)-4-haphyl-5-(2- naphthylmethyl)piparszzes-2,3-dkons)	5.4	5	,1	2
34	Frocol-2-Naprithylalanthal Frocol-2-Naprithylalanthal (Alpha-Alpha-Trifluoro-m-Tolvi) acetic acid)	559.8	699.3	(SS)-1-((1S)-2-(benzylemino)-1-(2-naprityemethyl)edhyl)-5-(2- naphthylmethyl)-4-(2-(3-(billiannamethyl)phenyl (ethyl)pipperazine-2,3-done	6.1	5	1	2
35	imog 1, 2-Naphthylatanne (F mod 1, 2-Naphthylatanine (6-lent-8-tht-cyclotheranecarpoxyric acid)	579.9	679.4	(55)-1-(15)-2-(benzylumina)-1-(2-naphby) (methyl)ethyl)-4-(4-tan- buytzyczohazy) (methyl)-5-(2-naphthylmethyl) (plparazina-2,3-dione	6.1	5	1	2
28	mod.4.2-Mapritrialarine (Fmod.4.2-Naonthriusiane (Fm. Torrispetio soci)	545.8	945.3	(\$\$)-I-([15]-2-(benty/temino)-I-(2-napithy/methy/)ethyl]-4-(2-(3-methy/pnery/)ethyl]-5-(2-napithy/methyl)pperazzne-2,3-done	5.6	. 5	1	2

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Docket No.: 66821-058

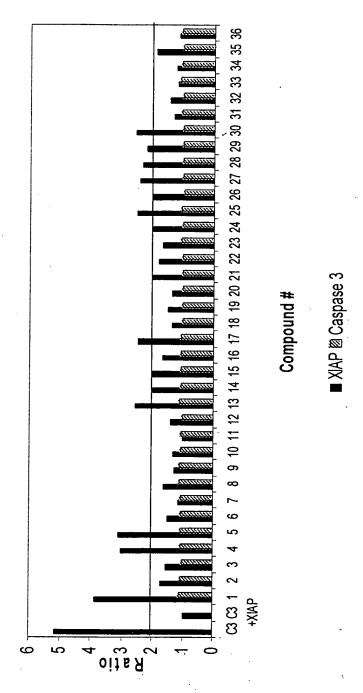
55/123



TPI 1391 1-36

FIGURE 23B





TPI 1391 1-36

FIGURE 23C

Title: METHODS AND COMPOSITIONS FOR...

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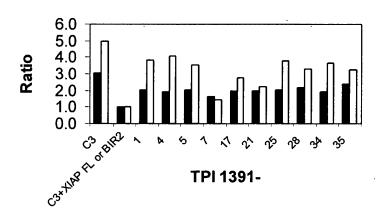
Selected TPI 1391

TPI 1391	_	e 3-XIAP 0 (μM)
	10-3	υ (μινι)
	AVG	STD
1	29.6	2.9
4	28.0	2.1
5	29.9	2.5
7	>162	
17	57.3	16.1
21	33.6	0.7
25	29.0	2.8
28	25.1	5.9
34	39.4	0.5
35	32.6	1.2

FIGURE 23D

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1

■ XIAP-FL □ XIAP-BIR2

FIGURE 23E

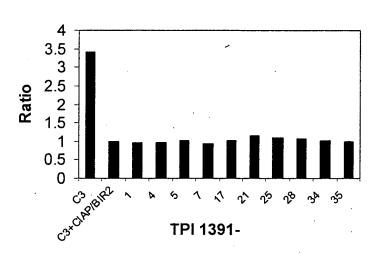


FIGURE 23F

TP11400	Structures FIGURE 24A	MW	Exact Mass	Name	MLogP	HBandAcceptor	HBandDonar	RuleOfFiv=
1	Boc-L-Cvclohexylataninef4-Biohenviacetic scidf4-Ethoxyphenviacetic scidf	606.9	806.4	N-(3-((25,55)-1-(2-(1,1'-biphenyt-4-yl)ethyl)-5- (cyclohexytmethyl)-2.3,5,6-tetrahydro-1H- imidazo(1,2-ejinidazo-2-yrjpropyl)-2-(4- ethoxypnenyl)acetamide	5.8	đ		2
2	Boc-L-Cyclohexylatanine IPhenylacetic acid[4-Ethoxyphenylacetic acid]	530.8	530.4	N-(3-{(25,55)-5-(cyclohery/methyl)-1-(2- phenylethyl)-2,3,5,8-letrahydro-1H-imidazo(1,2- a lmidazol-2-yl propyl)-2-(4-ethoxyphenyl)acetami	4,7 Je	6	1	2
3	[Boc-L-Cyclohexytalanine]]4-Phenylbutyric acid]]4-Ethoxyphenylacetic acid]	558.8	558.4	N-(3-((23,55)-5-(cyclohexylmethyl)-1-(4- phenylbutyl)-2,3,5-letranydro-1H-imidazo(1,2- a[midazol-2-yl]propyl]-2-(4-ethoxyphenyl)acetami	5.1 Ia	5		2
4	[Boc-L-Cyclohevylalanine#Heptanoic scid#4-Ethoxyphenylacetic acid]	524.8	524.4	N-{3-{(2\$,5\$}-5-{cyclohexylmethyl}-1-heptyl-2,3,5, tetrahydro-1H-imidazof1,2-a imidazol-2-yl propyl}- (4-ethoxyphenyl)acetamide	3- 2- 4.8	đ	1	. 2
5	[Boc-1-Cycloheryfalanine]Cyclohexanecarboxylic scid[14-Ethoxyphenyfacetic scid]	522.8	522.4	N+(3+((25,55)-1,5-bis(cyclohexylmethyl)-2,3,5,8- tetrahydro-1H-limidazo(1,2-a]imidazo-1-2-r/lpropyl)- (4-ethoxyphenyl)acetamide	2- 4.8	g g	1	2
đ	[Boc-4Cyclohexylalanine [4-tert-Butyl-cyclohexaneca/Doxylic acid][4-Ethoxyphenylacetic acid]	578,9	578.5	N-(3-{(25,55)-1-{(4-tent-budykcyclohexyf)methyf)-5 (cyclohexyfmethyf)-2,3,5,8-terahydro-1H- imidazo(1,2-afmidazot-2-yf)propyf)-2,4- ethoxyphenyf)acetamide	5.5	5	1	2
7	Boot - Cyclonexylainine 1 - Adamentaneacetic scid 4-@thoxyphenylacetic scid	588.9	588.4	N-(3-((25,55)-1-(2-(1-adamantyl)ethyl)-5- (cyclonexylmethyl)-2,3,5,8-letrahydro-1h- imidazo(1,2-a imidazo(-2-yi)propyl)-2-(4- ethoxyphenyl)acetarriide	5.7	đ	1	2
8	Boc-D-Cyclonexylatanine (4-Slohenviagetic acid (4-Ethoxyphenylacetic acid)	606.9	506.4	N-{3-{(28,5R}-1-{2-{1,1'-biphenyk-4-y)jethyl -5- (cyclonexylmethyl)-2,3,5-2-etrahydro-14- imidazo(1,2-a midazok-2-y propyl)-2-{4- ethoxypnenyl)acetarnide	5.6	5	1	2

TP1140	0 Structures FIGURE 24A	I MW	Exact Mass	Atom-	T 10 -	T.:.		
		MYV	=xact Mass		MLoaP	HBondAcceptor	HBondDonor	RuleOfFive
9	[Bac-Q-Cyclohexylalanine Phenylacatic acid] 4-Ethoxyphenylacatic acid]	530.8	530.4	N-1-3-(28,5R)-5-(cyclonexylmethyl)-1-(2- phenyletnyl)-2,3,5,8-letrahydro-1H-imidazo(1,2- a midazol-2-ylipropyl)-2-(4-ethoxypnenyl)acetami	4.7 da	đ	1	2
10		558.8	558.4	N-(3-((25,5R)-5-(cyclohexylmethyl)-1-(4- phenylbubyl)-2,35,9-letrahydro-1H-imidazo(1,2- allmidazot-2-ylproyl)-2(4-dhoxyphenyl)-acetami	5,1	5	1	2
	(Boc-O-Cyclohexytalanine)(4-Phenylbutyric acid)(4-Ethoxyphenylacetic acid)			an instance yiping it a 4-euloxyoneryijacetami				
11		524.8	524.4	N-[3-[(25,5R)-5-(cyclohen/methyl)-1-heplyl-2,3,5,6 tetranydro-1H-imidazo(1,2-a imidazol-2-h]propyl)- (4-ethoxyphenyl)acatamide	2- 4.8	6	1	2
	IBoc-Q-Cyclohexylalanine Heptanoic acid 4-Ethoxyphenylacetic acid					-		
12		522.8	522.4	N-(3-((23,5R)-1,5-bis(cyclohexylmethyl)-2,3,5,6- tetrahydro-1H-imidazo(1,2-a jimidazoh-2-yilpropyl)- (4-athoxyphenyl)acetamide	- 4.8	6	1	2.
<u> </u>	[Boc-D-Cyclohexylalanine][Cyclohexanecarboxylic acidl[4-Ethoxyphenylacetic acid]	i i	,		· ·			
13		578.9	578.5	N-(3-((2S.5R)-1-((4-tert-buty/cyclohexyf)methyf)- (cyclohexyfmethyf)-2,3,5,6-tetrahydro-1H- imidazo(1,2-a)jmidazol-2-yf)propyf)-2-(4- athoxyphemyf)acetamide	5.5	6	.1	2
	Boc-D-Cyclohexyfalanine 4-tert-Butyf-cyclohexanecarboxylic acid 4-Ethoxyphenylacetic acid (-			·
14	[Boc-O-Cyclohexylalanine [1-Adarmantaneacetic acid] 4-Ethoxyphenylacetic acid]	586.9	S88,4	N-(3-(28,5R)-142-(1-adamentyl)ethyl)-5- (cyclonerylmethyl)-2, 3, 6-tetrehydro-1H- imidazo(1,2-s jimidazol-2-yjpropyl)-2-(4- ethoxyphenyljacetamide	5.7	đ	1	2
15	Boc 1. Nephthylalanine (4-Biphenylacatic acid (4-Ethoxyphenylacatic acid)	650.9	650.4 n	N-(3-(125,53)-1-(2-(1,1'-bipnenyi-4-yi)ethyi)-5-(2 aphthyimethyi)-2.3,5-4etranydro-11-imidazo(1,2- imidazo(-2-yi propyi)-2-(4-ethoxyphenyi)acetamije	5.9	6	. 1	2
	Solve province actual			2-(4-ethoxyphenyl)-N-(3-((25,55)-5-(2-				
18	Boc-L-Naphthvisianine TPhenylacetic acid Y4-Ethoxyphenylacetic acid]	574.8	574.3	naphthylmethyl)-1-(2-pnemylethyl)-2.3,5,8- tetrahydro-1H-imidazd 1,2-allmidazol-2- yl[propyl)acatamide	5.1	5	1	2

Title: METHODS AND COMPOSITIONS FOR...

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058

TP114	0 Structures FIGURE 24A	MW	Exact Mas	1 Name	· ··· -	Lun:		
		1	Gradinas	Same	MLogP	dBandAcceptor	HBondDonor	RuleOfFive
17	[Boc-L-Naghthyfalanine [4-Phenyibutyric scid][4-Ethoxyphenyiacetic acid]	602.8	602.4	2-(4-ethoxypheny)-N-(3-((25.55)-5-(2- nephthytmethy)-1-(4-phenylbury)-2,3,5,8- tetrahydro-11-inidazo(1,2-alimidazoi-2- ylipropyl)acetamide	5.4	8	1	2
18	[Boc-1-Neghthylalanine Frieptanoic acid [4-Ethoxyghenylacetic acid]	568.8	568.4	2-(4-ethoxyphenyl)-N-(3-((25,58)-1-heptyl-5-(2- naphthylmethyl)-2,3,5.8-tetrahydro-1H-imidazo(1, a]imudazol-2-yi[propyi]acetamide	J- 5,1	6	1	2
19	[Boc-L-Naghthylalanine][Cyclohexanecaroxylic acid][4-Ethoxyphenylacetic acid]	S68.8	566.4	N-(3-((25,55)-1-(cyclohexylmethyl)-5-(2- naprthylmethyl)-2,3,5-letranydro-1H-imidazo(1,3 e imidazol-2-ylipropyl)-2-(4-ethoxyphenyl)acetamia	- 5.1 ·	6	1	2
20	[Boc-1-Naphthylalanine][4-tert-Butyl-cyclohexanecarboxylic acid][4-Ethoxyphenylacetic acid]	622.9	622.4	N-{3-{(25,55)-1-{(4-tert-butyk-ycionexyl)medryl}-5-{2- nephthylmethyl}-2,3,5,8-tertahydro-1H-lmidazof 1,3 a]lmidazol-2-yl propyl)-2-{4-ethoxyphenyl acetamia	5.8	6	í	2 '
21	[Boo-L-Naphthylalanine] I -Adamaritaneacatic acid [4-Ethoxyphenylacetic acid]	632.9	632.4	N-(3-((2S,5S)-1-(2-(1-adamantyl)ethyl)-S-(2- naphthylmethyl)-2,3,5,4-letrahydro-1H-imidazd1,2- a]lmidazol-2-yl[propyl)-2-(4-ethoxyphenyl)acetamie	d ,0	đ	1	2
22	Bac-Q-Naphthylalanine #4-Biphenylacatic acid #4-Ethoxyphenylacetic acid]	650.9	650.4	N-(3-((2S,SR)-1-(2-(1,1'-biphenyl-4-yl)ethyl)-5-(2, naphthylmethyl)-2,3,5,6-tetrahydro-1H-Imidezo(1,2- ajimidazol-2-yi]propyl)-2-(4-ethoxyphenyl)acetamile	5.9	đ .	1	2
23	God-Q-Maghthylalanine Phenylacetic acid 14-Ethaxyphenylacetic acid	574.8	574.3	2-(4-ethoxyphenyl)-N-[3-[(25,5R)-5-(2- naprithyl(methyl)-1-(2-phenylethyl)-2,3,5,6- tetranydro-1H-imidazol1,2-ej/midazol-2- yl[propyl]-acetamide	5.1	a	1	2
24	8	502.8	802.4	2-(4-ethoxyphenyl)-N-(3-((2S, SR)-S-(2-naphthylmethyl)-1,(4-phenybusyl)-2,3,5-s-tetrahyoro-i-l-i-midazo(1,2-ejlmidazoi-2-yijpropyl)acetamide	5,4	8	1	2

TPI140	Structures FIGURE 24A	MW	Exact Mas	Name	MLogP	HBondAcceptor	HRandDonor	PutaOffice
25	9oc-D-Naonthylalanine#Heptanoic acid]4-Ethoxyohenylacetic acid]	568.8	568.4	2-(4-ethoxyphenyl)-N-(3-((25,5R)-1-heptyl-5-(2- naphthylmethyl-2,3,5,6-teranydro-1N-imidazo(1, alimidazol-2-ylipropyljecetemide		6		2
25	[Bac-O-Naphthylalanine [Cyclohexanecarboxylic acid [-Ethoxyphenylacetic acid]	588.8	566.4	N-(3-((25,5R)-1-(cyclonexylmethyl)-5-(2- naphthylmethyl)-2, 3, 5-tetrahydro-1H-imidazol ; alimidazol-2-yilpropyl)-2-(4-ethoxyphenyl)acetami	- 5.1 le ;	đ	1	2
27	[Boc-Q-Nasphthylalanine]4-lert-Butyl-cyclonexanecarboxylic acid[4-Ethoxyphenylacetic acid]	622.9	522.4	N-(3-((2S,5R)-1-((4-tent-butylcyclohexyl)methyl)-5-(2 naphthylmethyl)-2.3,5,6-tetrahydro-11-(-midazo(1, a imidazo(-2-yl propyl)-2-(4-ethoxyphenyi)acetami	2- 5.8 10	6	1	_ 2
28	[Boc-O-Nephthvialanine]1-Adamantanescetic scid]14-Ethoxyphenviacetic acid]	632.9	632.4	N-(3-{(25,5R)-1-{2-(1-adamantyl)ethyl}-5-(2-naphthylmathyl)-2-(3,5-8-etranydro-11-4-midazo(1,5-a)midazo4-2-ylipropyl)-2-(4-ethoxyphenyl)acatamid	. 8.0 e .	6	1	2
	Structures							
29	IBoc-L-Cyclohexylalanines I Phenylacetic acid [Phenylacetic acid]	488.7	485.3	N-[3-[(25,58)-5-(cyclohexylmethyl)-1-(2- phenylethyl)-2,3,5-6-letrahydro-1h-imidazo(1,2- a lmidazol-2-yi propyi)-2-phenylacetamide	4.9	5	1	1
30.)	(Bac-Q-Cyckhexyfalanine#Phenylacetic acid[Phenylacetic acid]	486.7	486.3	N-(3-{(2S.5R)-S-(cyclohexylmethyl)-1-(2- phenylethyl)-2,3,5,8-setranydro-11-inicazo(1,2- s midazol-2-yi propyl)-2-phenylacetamice	4.9	5	1	1
31	(Boc-Q-o-Chlore-Phenylalanine#Phenylacetic acid Phenylacetic acid	515,1	514.2	N-(3-((25,5R)-5-(4-chlorobenzy))-1-(2-phenylethyl)- 2,3,5,8-tetrahydro-1H-imidazo(1,2-a)midazol-2- yl]propyl)-2-phenylacetamide	5.1	5	. 1	2
32	Boc-Q-e-Fluoro-Phenylalanine (Phenylacetic acid)	498.8	498.3	N-(34(25,5R)-5-(4-fluoropenzyi)-1-(2-phenylethy)- 2,3,5,8-4etrahydro-1H-imdazo(1,2-ejimidazok2- yi[propyj]-2-shenylacetamide	5.0	5	1	1

TP11400	Structures FIGURE 24A	MW	Exact Mass	Name	MLogP	HBondAcceptor	HBandDanar	RuleOfFixe
. 33	IBoc-L-o-Fluoro-Phenyialanine IPhenylacetic, acidi Phenylacetic, a	498.8	498.3	N-(3-((25.55)-5-(4-fluorobenzyl)-1-(2-phenylethyl 2,3,5,6-tarranydro-1H-imidazo(1,2-jirnidazok-2- ylipropyl)-2-pnenylacatamide	5. 0	5	1	1
34	(Bac-0-2-Chloro-Phenylalenine) Phenylacetic acid (Phenylacetic acid)	515.1	514.2	N-(3-((2S, SR)-5-(2-chlorobanzyl)-1-(2-phenylethyl 2,3,5,8-tetrahydro-1H-midazol1,2-ejimidazol2- ylipropyl}-2-phenylacetamide	5.1	5	1	2
35	(Soct-O-Ethyl-Tyrosine)(Phenylacetic acid)	524.7	524.3	N-{3-{(2S,SS)-5-{4-ethoxybenzyi}-1-{2-phenylethy 2,3,5,6-tetranydro-1H-imidazol1,2-ajimidazol-2- yijpropyi}-2-phenylacetamide)- 4.5	5	,	2
36	[Boc-D-O-Elhyk-TyrosineijPhenylacetic acid]	524.7	524.3	N-{3-{(2S, SR}-S-(4-ethoxybenzyl)-1-{2-phenylethy 2,3,5,6-tetranydro-1H-driddaxd[1,2-e]imidazol-2- yl[propyl]-2-phenylacetamide)- 4.5	8	1	2
37	[Boc-D-O-Methyl-Tyrosine [Phenylacedc, acid] Phenylacetic, acid]	510.7	51 0.3	N-(3-{(29,5R}-5-(4-methoxybenzyi)-1-(2- phenyiethyi)-2,3,5-tetrahydro-11-4-midazo(1,2- a]imidazol-2-yl[propyi]-2-phenylacetamide	4.3	6.	1	2
38	(Boc-L-3,5-Diado-Tyrosine(B/Z)[[Phenylacetic acid]	748.4	748.1	N-{3-{(29, 55)-5-{4-hydroxy-3,5-dilodobenzyi}-1-{2- phenylethyl)-2,3,5,6-tetrahydro-1h-l-midazo(1,2- a]lmidazol-2-yi]propyi]-2-phenylacetamide	5.4	đ	2 .	2
39	Boc-1-Naonthvialanine (Phenylacetic acid)	530.7	530.3	N-(3-((2S, SS)-5-(2-naphthytmethyl)-1-(2- phenylethyl)-2, 3, 5, 6-tetrahydro-1H-Imidazo(1,2- a jimidazol-2-yilpropyl)-2-phenylacetamide	5.2	5	1	2
40	Boc-D-Naphthvialanine #Phenylacetic acid[Phenylacetic acid]	530.7	530.3	N=(3-{(25,5R)-5-(2-napnthylmethyl)-1-(2- phenylethyl)-2.3,5,6-tetranydro-11-i-midazo(1,2- a imidazo1-2-yl[propyl]-2-phenylacetemide	5.2	S	1	2

TPI1400	Structures FIGURE 24A	I MW	Exact Mass	Name	MLagP	HBondAcceptor	HBondDonor	RuleOfFive
41		55ø.8	556.3	N-(3-((25,55)-5-(1,1'-biphenyl-1-ylmethyl)-1-(2- phenylethyl)-2,3,5,6-tetrahydro-1H-imidazo(1,2- a imidazol-2-yljpropyl)-2-phenylacetamida	5.5	5		2
	Boc-L-4.4'-Biphenvi-Alanine Phenviacetic acid Phenviacetic acid	Ĺ <u>.</u>						
	Structures							-
42	Bac-L-Phenvisianine (p-Tolviscetic acid (Phenviacetic acid)	494,7	494,3	N-(3-((23,55)-5-benzyl-1-(2-(4-methylphenyl)ethy 2,3,5,6-tetrahydro-1H-imidazo(1,2-ajimidazol-2- yf)propyl)-2-phenylacetamide	}- 4.8	5	. 1	1
43	[Boo-L-Phenylalanine] 4-Favorophenylacetic acid[Phenylacetic acid]	498.5	498.3	N-(3-((25,55)-5-benzyl-1-(2-(4-fluorophenyl)ethyl 2,3,5,6-tetrahydro-1H-imidezof 1,2-a jimidezol-2- yi)propyl)-2-phenylacetamide	5. 0	-5	1	1
44		\$10.7	\$10.3	N-(3-((25,55)-5-benzyl-1-(2-(3- methoxyphenyi)ethyl-2,3,5,6-tetrahydro-1H- imidazo(1,2-aljmidazol-2-yl)propyl)-2- phenylacetamide	4.3	G	1	.2
45	(3oc-L-Phenylalanine [3-Methoxyphenylacetic acid[Phenylacetic acid]	510.7	510.3	N-(3-((28,58)-5-benzy)-1-(2-(4- methoxypheny)ethyl;2,3,5-letrahydro-1H- imidazo(1,2-e midazo(2-yl)propyi)-2- phenylacetamide	4.3	5	1 7	2
46	Boc-L-Phenylalanine [4-Methoxyphenylacetic acid [Phenylacetic acid]	524.7	524.3	N-(3-((25,55)-5-benzy)-1-(2-(4-ethoxyphenyl)ethy) 2,3,5,6-terahydro-1H-imdazo(1,2-ejimidazoi-2- yljpropyl)-2-phenylacetamide	- 4.5	đ	1	2
47	Boc-L-Phenylatanine (4-Biphenylacetic acid [Phenylacetic acid]	556.8	556.3	N-(3-((29,58)-5-benzyl-1-(2-(1,1'-biphenyl-4- y) ethyl)=2,3,6-tetrahydro-1H-imidacq(1,2- a imidazol-2-yi propyi)-2-phenylacetamide	5.5	5	1	2
46	Boc 4-Phenylalanine [4-Phenylbutync acd [Phenylacatc acid]	508.7	508.1	N+(3-((25,59)+5-benzy)+1-(4-phenylbutyl)-2,3,5,8- tetranydro-1H-imsazo(1,7-ejimsdazo+2-yi[propyl)-2 phenylacatamude	- 5.0	5	1	2

701140	Cineture EIGUDE 244		~·-					•
1711400	Structures FIGURE 24A	MW	Exact Mas	Name	MLogP	HBondAcceptor	HBondDonor	RuleOfFive
49	[Boc-L-Phenylalanine [Hegtanoic acid] Phenylacetic acid]	474,7	474.3	N-{3-{(23,55)-5-hanzyl-1-haptyl-2,3,5,8-tetranydr 1 H-imidazo(1,2-ajimidazol-2-yljpropylj-2- phenylacetarride	4,7	s	1	. 1
50	IBoot-Phenylaianine (3-Methylvaleric scid [Phenylacetic scid]	460.7	480.3	N-(3-((2S,5S)-5-benzyl-1-(3-methylpentyl)-2,3,5,6 latrahydro-1H-imidazd (1,2-ajmidazol-2-yijpropyl)- phenylacetamide	- 2- 4.5	5	1	1
51	[Soc-1Phenylalanine] 4-Methylvaleric acid] [Phenylacetic acid]	.450.7	460.3 	N-[3-[(25,58)-5-benzy -1-(4-methylpentyl)-2,3,5,5 tetrahydro-1H-imidazo(1,2-a]imidazo(-2-yi]propyl- phenylacetamide	- 4,5	5	,	1
52	Siructures	556.8	556.3	N-(3-((25,55)-5-banzyl-1-(2-phenylethyl)-2,3,5,6 tetrahydro-1H-midszo(1,2-s[midszo-1-2-yl]propyl)-2 (1,1'-biphenyl-4-yl]acetamide	- 5.5	S	1	2
53	Boc-L-Phenylalanine (Phenylacetic acid (4-8) ohenylacetic acid)	472.7	472.3	N-(3-((23,53)-5-benzyl-1-(2-phenylethyl)-2,3,5,8- tetralnydro-11-imidazo(1,2-a jmidazol-2- ylipropyl(cyclohexanecarboxamide	4.7	5	1	t
54	Boct_Phenylalanine I Phenylecatic acid I Cyclohexaneacatic acid [485.7	485.3	N-{3-{(25,55)-5-benzyl-1-{2-phenylethyl)-2,3,5,6- etrahydro-1H-imidazof (,2-a)midazo-2-yl[propyl)-2- cyclohexylacetamide	4.9	Š	1	1
55	20c1_Phenylalanine (Phenylacetic acid (Cyclohexanebutync acid)	514.8	514.4 t	N-(3-{(25,55)-5-benzy+1-(2-phenylethyl)-2,3,5,6- etrahydro-1H-imidazof (2-a]midazot-2-ylipropyl)-4- cyclohexylbutanamide	5.2	s	1	2
56	OC.1Phenylalanine Phenylacatic acid Cycloheptanecarboxyric acid	486.7	485.3	N-(3-((25,55)-5-benzy-1-(2-phenylethyl)-2,3,5,8- tstrahydro-1H-imdazd1,2-a jmidazd-2- yljpropyl-cycloneptanecarboxamide	4.9	. ·	1	1

TP11400	Structures FIGURE 24A	MW	Exact Mass	Name	MLogP	HBondAcceptor	HBondDonor	- alloge
57	[Boc-t_Phenylalanina [Phenylacetic acid]3-Cyclopentyloropionic acid	486.7	486.3	N-(3-((25,58)-5-benzyl-1-(2-phenylethyl)-2,3,5,6 letrahydro-1H-imidazd(1,2-a imidazol-2-yl propyl)- cyclopenfylpropenamide		5	1	RUBOTEME
58	(Boott-Phenylalarine#[Phenylacetic acid#3.5-bis-(Triffuoromethyl)-phenylacetic acid	616.6	616.3	N-(3-((25,55)-5-benzyl-1-(2-phenyletryl)-2,3,5,6 tetrahydro-1H-Imidazo(1,2-a midazol-2-yi propyl- (3,5-bis(trifluoromethyl)phenyl acetamide	2- G .4	5	1	2

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058 68/123

TPI 1400 1-28

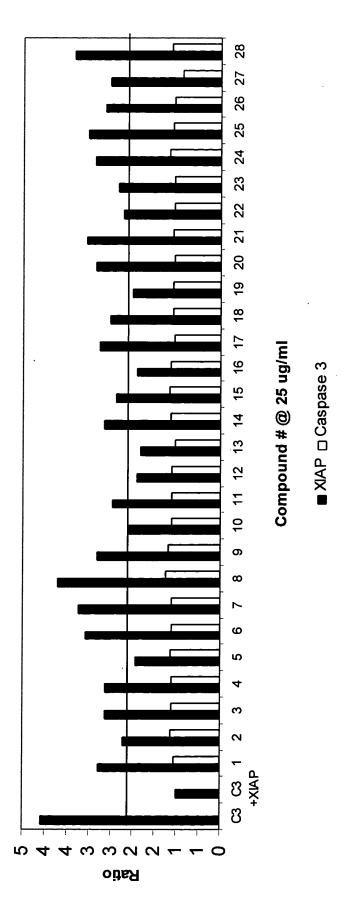


FIGURE 24B

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058 69/123

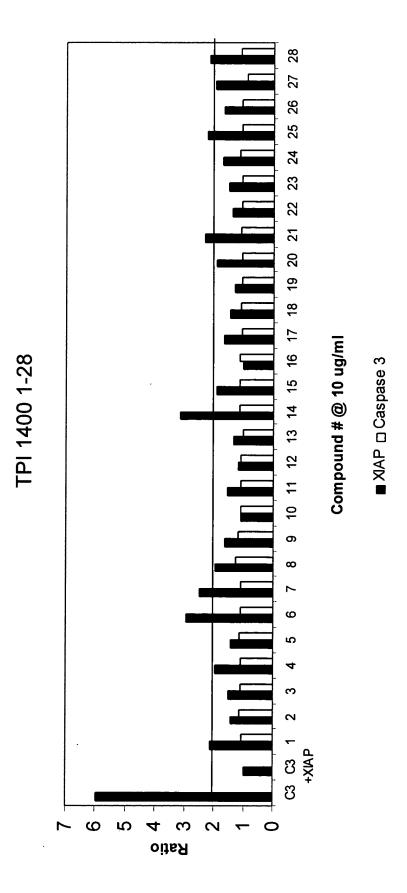
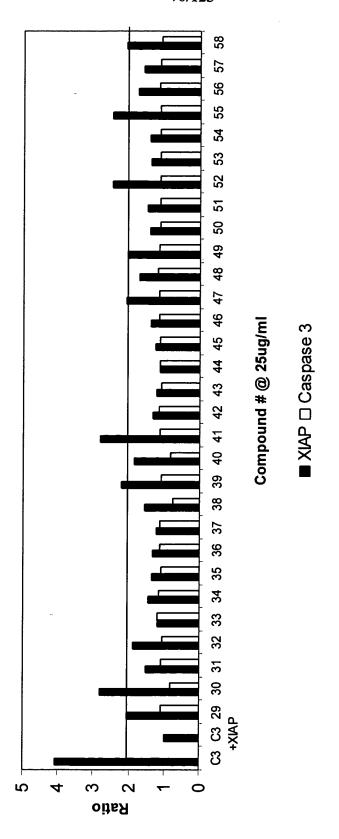


FIGURE 24C

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TPI 1400 29-58

FIGURE 24D

Title: METHODS AND COMPOSITIONS FOR... Inventors: Reed et al.

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058 71/123

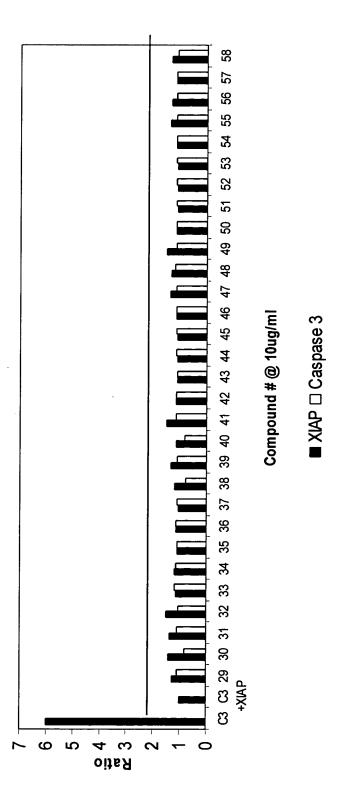


FIGURE 24E

Title: METHODS AND COMPOSITIONS FOR... Inventors: Reed et al.

Filed: Herewith
Docket No.: 66821-058
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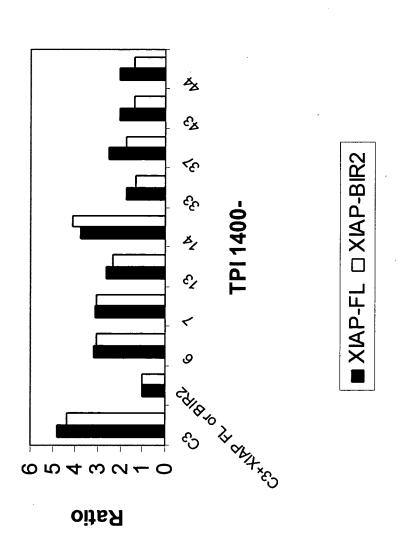
Selected TPI 1400

TPI 1400-	Caspa IC-50	se 3-XIAP (μM)
	AVG	STD
6	26.6	4.6
7	40.2	8.7
14	31.2	6.8
13	157.2	
33	>200	
37	157.6	
43	169.5	
44	120.2	

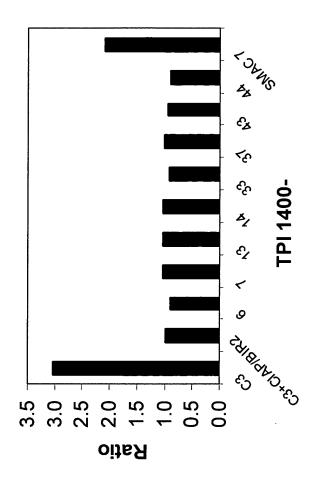
FIGURE 24F

Title: METHODS AND COMPOSITIONS FOR...
Inventors: Reed et al.
Filed: Herewith

Docket No.: 66821-058

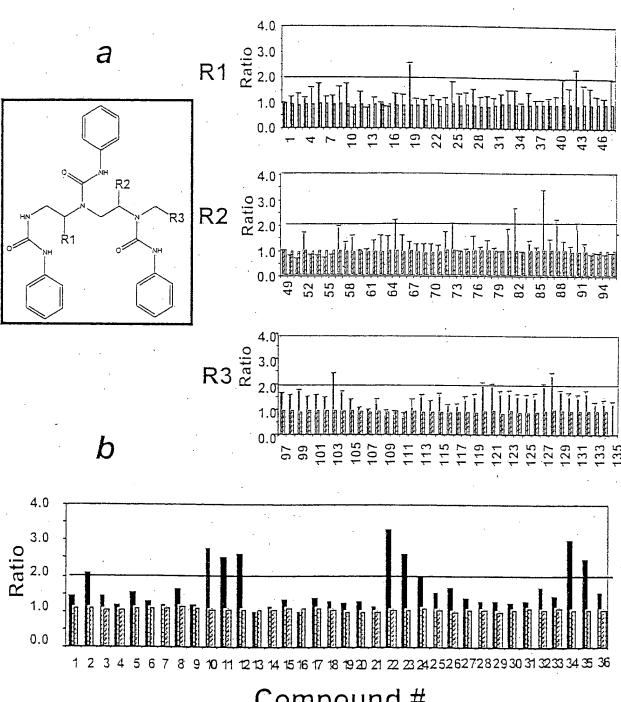






100 µg/ml 10, 2003

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058 75/123



Compound #

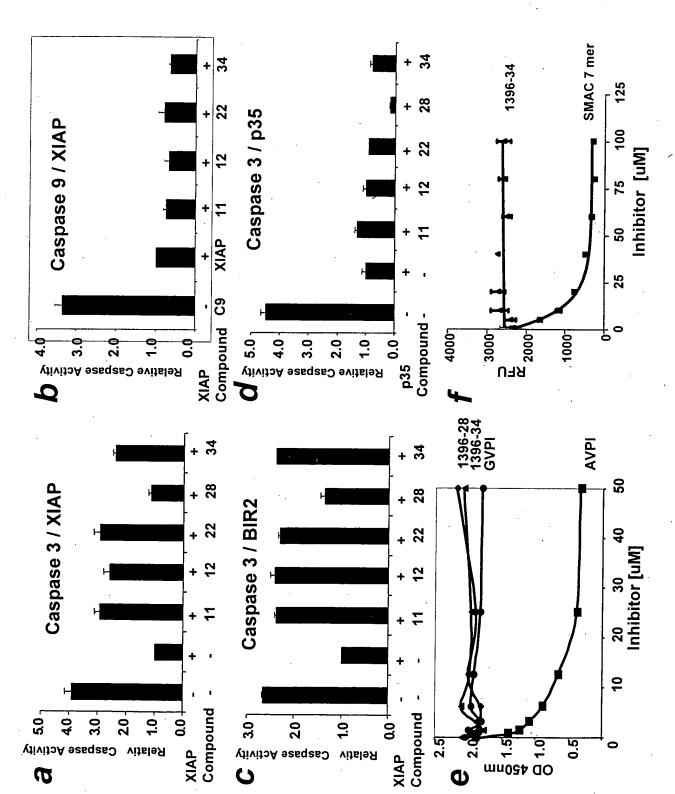
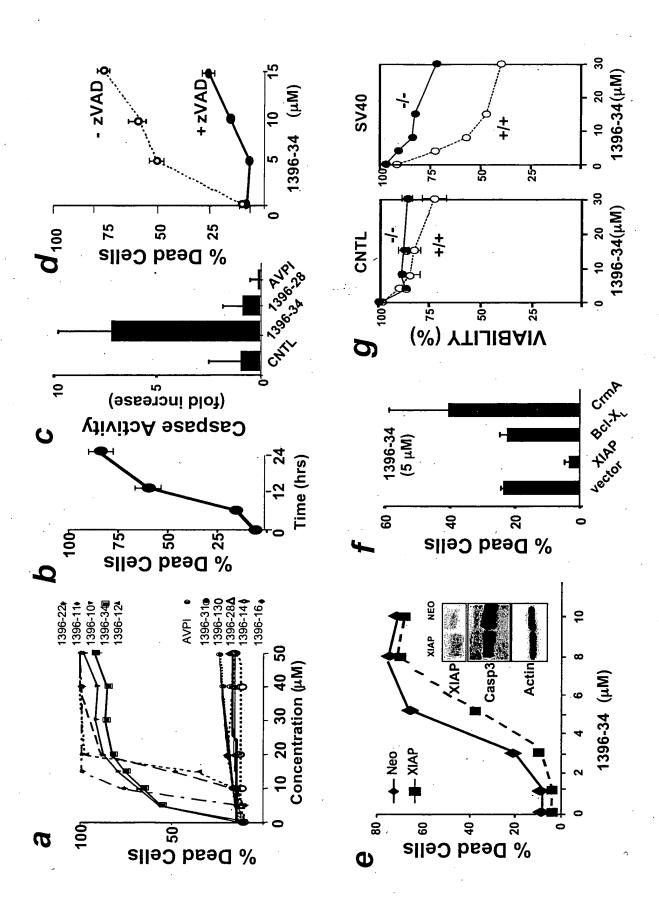
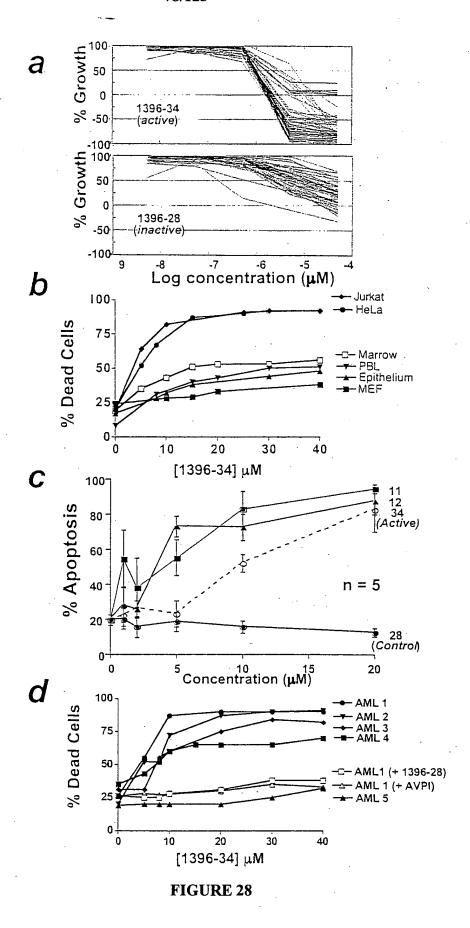
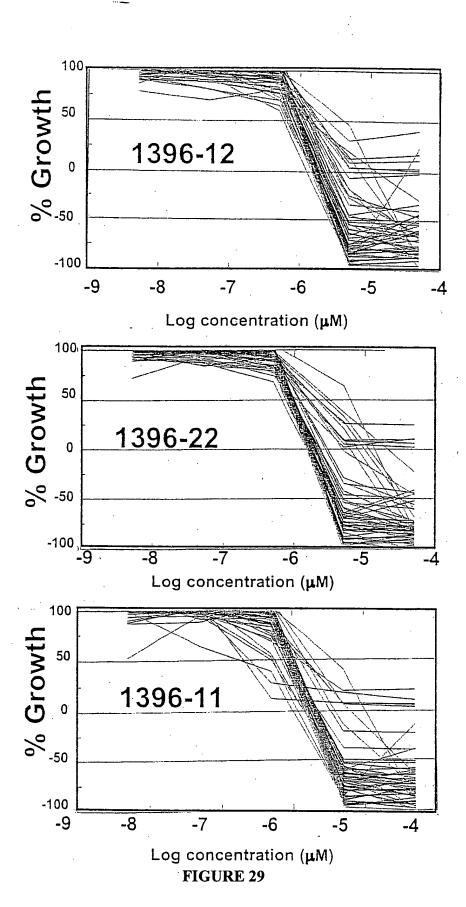


FIGURE 26









Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058 80/123

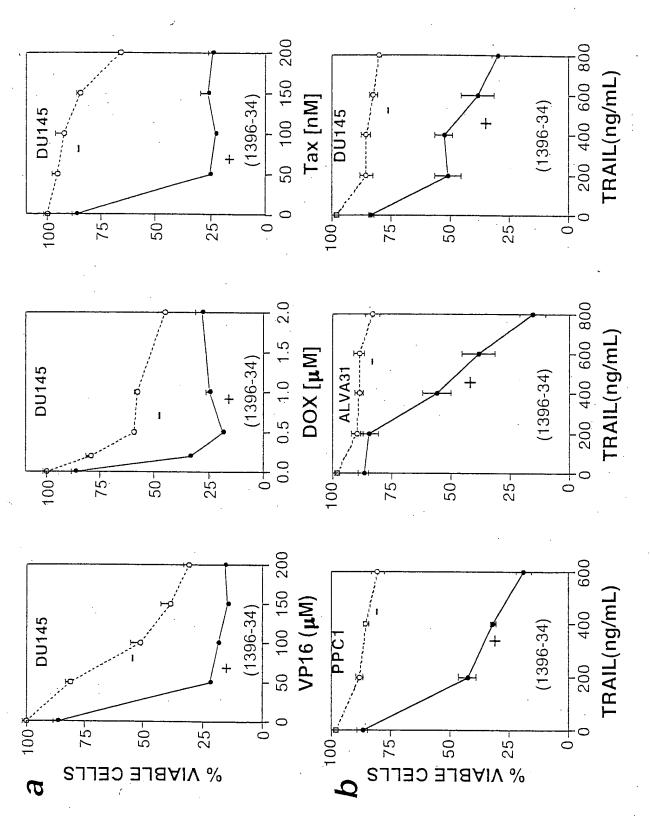


FIGURE 30



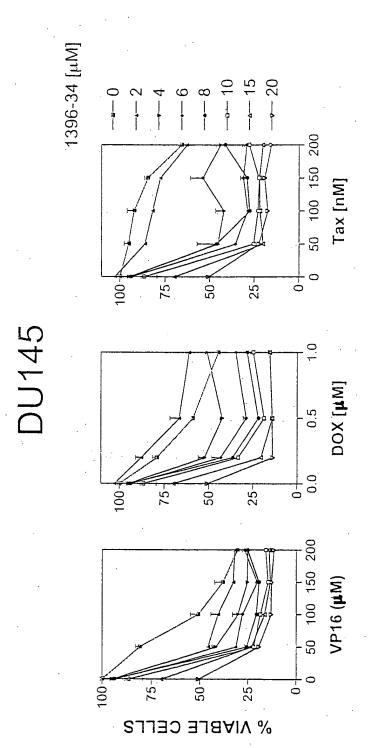
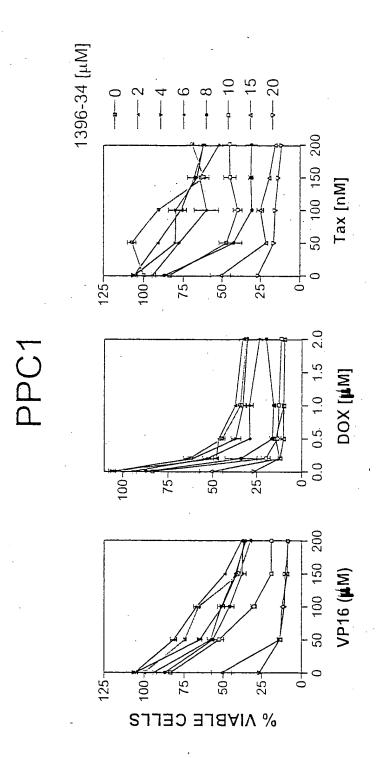
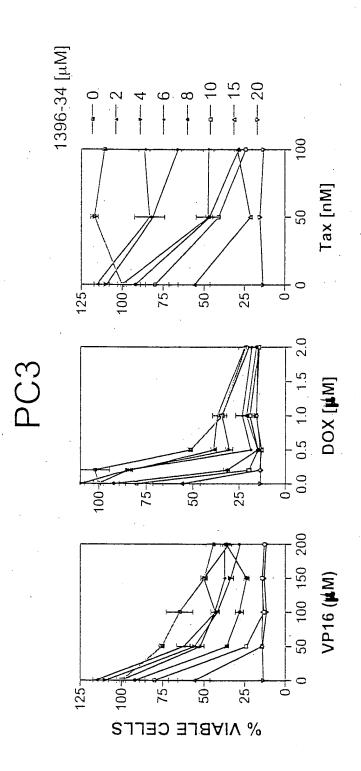


FIGURE 31A

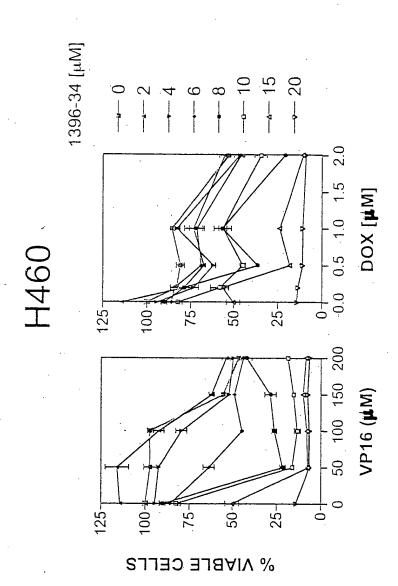


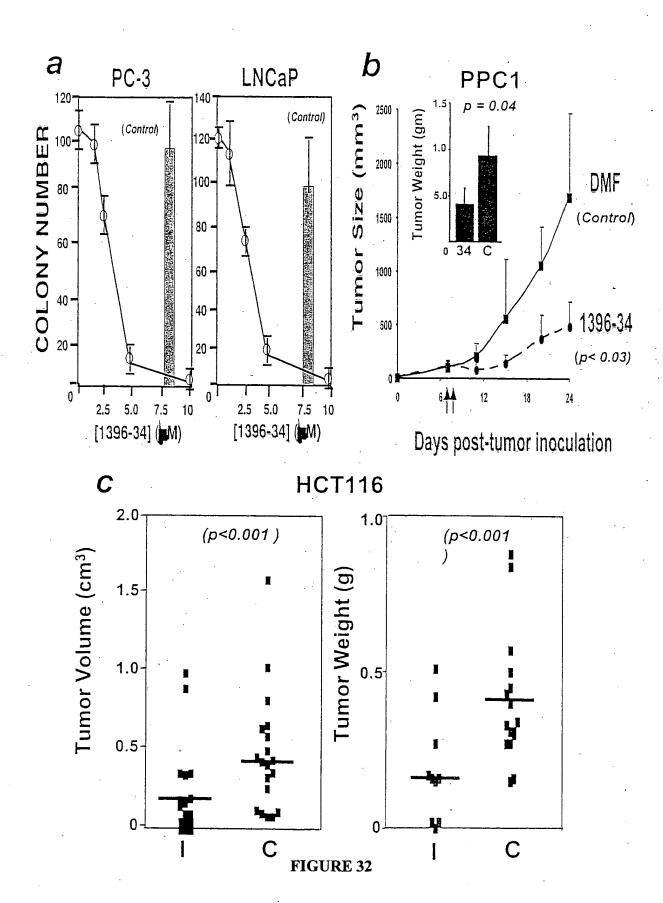


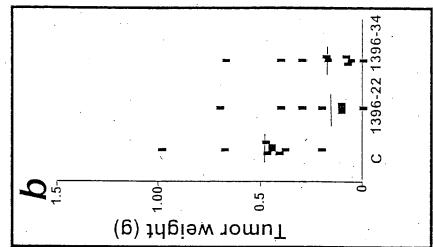


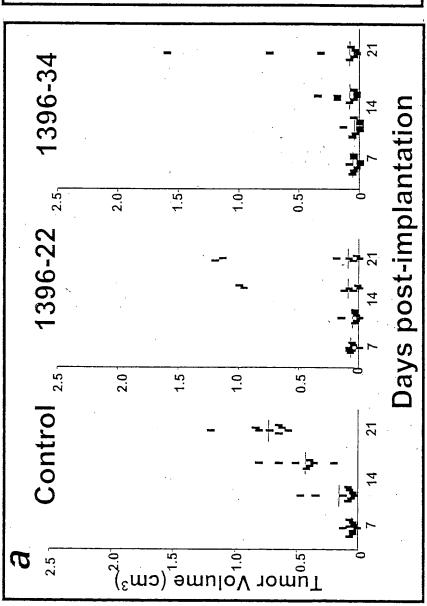












10:	Name	MW.	i Structure	Reiguve cascase 3 activity i @ 25 ug/mi	lligwesti ug/m² "I
TPI 1505-:'	N-I(SA)-6-I(aniinocaroonyi)aminol-5-I(aniinocaroonyi)(((2A)- 1-12-4-metnoxypnenyijetnyljpyrrolidin-2- yl)metnyi)aininojhexyl)-N-metnyl-N-phenyturea	719.2		2.2	3.25
TP! 1509-2	N-{((2R)-1-{2-{1-acamanıylethylovrolidin-2-yil methyl)-N- {{1f}-1({(anilinocaroonyl)amnolmethyl)-5- ((anilinocaroonyl)(methyr)amino)pentyl-Nohenyuraa	7 48. 0	0-1,10	2.5	12.5
TPI 1509-3	N- (5F)-6- (anilinocarbonyl)amino -5-((anilinocarbonyl) ((2F)- 1-(4-5)d0hexyibutyl)pyrrolidis1-2-yl me(nyl)amino)hexyl -N- inernyl-N-pnenylurea	. · . 724.0	0-:T; 0-:T;	2.4	12.5
TFI 1509-4	N-{(1S)-2-{(anilievocaroonyl)amino -1-{2- napr(hylmelbyl)erhyl-N-{((2R)-1-{2-4- metnozyphenyl)ernyl pyrrolidin-2-yl metnyl)-N'-phenylurea	655.8		2.4	25
TPI 1509-5	N-(((2F)-1-[2-(1-adamantyl)etnyl)pyrrolidin-2-yl)metnyl)-N- ((1S)-2-((anilirocarbonyl)arninoj-1-(2-nabrithylmetnyl)etnyl)- N-phenylurea	6.1.88		2.5	25
7P1 1509-6	N-{(1S)-2-{(aniiinocarsonyl)amino}-1- 2- naphthytmethyl)ethyl-N-{((2R)-1-(4- cyclonexylbutyljpyrroligin-2-yl[methyl]-N-pnenylurea	859.4		. 2.0	12.5
TP1:509-7	N- (18)-2- (anilinocarocnyi)amino -1- (cyclonexyimamylemyi -N- ((28)-1- 2-(4- memoxypnenyi)amyi pyrrolidin-2-yi)memyi)-N'-phenyiuraa	611. .3		. 2.4	25

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10 \$	Name	MW			
TPI 1509-8	N-{{(2R}-4-{2-{1 - ±damantyltetnyljpyrrolidin-2-yijimatnyli-N- {{(1R}-2-{taniinocs:roonyrjamino}-1-(cyclonexylmetnyltetnyl)- IV -onenyurea	539.9	Structure	3	ilosii uann
TPI 1509-3	N-{(1:3)-2-{{aniiinocarbanyi}amii;q -1- (cyclanexyineimyi)einyl -N-{((2:3)-1-(4- cyclanexyibutyi)pyrrolidii-2-yi memyi -N-qnenyiurea	815.9		2.2	25

Relative crisplase-3" activity in the XIAP deregnassion assay was calculated as the ratio of the Vmax in the presence of each compound divided by the Vmax of the controls having caspase-3 and XIAP. [fowest] ug/ml "" fowest concontration in which the relative caspase-3 activity was 1.8

	Cade: 1077		D-Cyclohexylalanine	, D-Proline	Lip	inski Alerts	: MW>500, MlagP > 4.15,	HBD>5, HBA>10	•
	Modifications of TPI1509-7			_					
	Structure	MW	Modification	R group	Yield (mg)	MLOGP	Hydrogen Bond Donors	Hydrogen Bond Acceptors	Lipinski Alerts
6	L-cyclohexylalanine analog	611.38	Sterochemistry	R1	54.3	4.26	3	8	2
7	L-Proline L-cyclohyylalanine analog	611.38	Sterochemistry	R1 and R2	54.4	4.26	3	8	2 ·
. 8	Q.F.	353.21	Removal of R1 and associated urea	·R1	14.8	2.63	2	5	0.
9	Split parent compound-Right side	394.24	Removal of R2 and R3	R2 and R3	32	3.02	4	6	0 -
10	0.1	477,31	Removal of R3	R3	5.6	3.29	4	7	0.
11	Remove R3-Acetyl substitution (ethyl)	505.3	Replacement of R3 with ethyl	R3	51.1	3.68	3	7	1
12	Remove R2-Giycine substitution	585,37	Removal of R2	R2	56.1	3.90	. 3	8	1
13	Remove R2-(0-Alanine) substitution	599,38	Replacement of pyrrolldine with N-metylalanine	R2	50.2	4.08	3	8	1
.14	Remove urea 2-methyl substitution	506.36	Removal of N-urea :	Urea	48.7	3.89	2	6	1
15	Remove R1-Glycine substitution	515.2	, Removal of R1	R1	'51.2	2.97	3	8	1
16	Remove R1-(0-Alanine) substitution	529.31	Replacement of R1 with methyl	R1	51.5	3.16	3 ,	8	1
17	Remove urea 1-methyl substitution	506.36	Removal of N'-urea	Urea	10.3	3.89	2	6	1
18	Remove ureas-benzoyi substitution	581.36	Replacement of phenylurea with phenylacyl	Urea	15.2	4.95	1	6	2
191	Remove ureas-acatylate	457.33	Replacement of phenylures with acetyl	Urea	. 18.8	3,01	. 1	6	o

20	Urea substitution-ethyl isocyanate	515.38	Replacement of phenylurea with ethylurea	Urea	53	2.71	3	. 8	1
21	Urea substitution—methylphenylisocyanate	639.41	Replacement of phenylures with pomethylphenylures	Urea	67.7	4.61	3	8	2
22	Urea substitution—fluorophenylisocyanate	647.36	Replacement of phenylurea with p- ; fluorophenylurea	Urea	72.2	4.70	.3	8	2
23	Urea substitution—nitrophenylisocyanate	701.35	Replacement of phenylurea with p-nitrophenylurea	Urea	66.4	4.39	3	14	3

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	Anne	Jurka	<u>5</u>	20	z				
		IC-50-MTT uM *** Jurka	MCF-7	>163	14.7 >163				
ĺ	TPIMS	IC-50-1	Jurkatt	10.8	14.7				
	ession*		R group 100 ug/ml 25 ug/ml IC-50 uM Summ activity Jurkatt MCF-7 IC-50	‡	‡				
(2-6)	AP derepr		IC-50 uM	36.0	57.2				
TPI 150	Caspase 3-XIAP derepression*	סייים של של מייים מביים מב	ıtio**	tio**	tatio**	Caspase 3-XI Ratio**	25 ug/ml	1.7	1.6
ylurea (Ü	Ra	100 ug/ml	2.4	2.2				
oly-phen			R group						
SAR of active poly-phenylurea (TPI 1509-7)			MW Modification	611.82 Native-R2=D-proline	R2=L-Proline				
			ĕ	611.82	611.82				
			Structure	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	**************************************				
			1540-	1 1509-7	1 1507 21 30 (TPI 396-34)				

	,			
N.T	6.3	>30	F.Z	T.N
7.4.7	15.5	18.4	247.0 259.3	155.1
9.8	11.5	15.4	247.0	53.5
‡	‡	‡	I	‡ .
39.3	97.0	102.0	>283	40.9
8.	4:	1.3	6.0	1.7
2.2	2	2	1.2	2.3
쥰	R1	R1	R1	R1 and R2
Sterochemistry	Removal of R1	Replacement of R1 with methyl	Removal of R1 and associated urea	Sterochemistry
611.38	515.2	529.31	353.21	611.38
Cyclohesylalarihe anekg	C C Fr C Fremove R1-Gycine substitution	O C C C C C C C C C C C C C C C C C C C	O C C C C C C C C C C C C C C C C C C C	C C C C C C C C C C C C C C C C C C C
ဖ	15	. 16	ю	7

12	Remove R2 Glycine substitution	585.37	Removal of R2	R2	2.2	1.6	54.7	#	43.9	43.9 >171	77
13	C F C C C C C C C C C C C C C C C C C C	599.38	Replacement of pyrrolidine with N-metylalanine	R2	2.3	1.7	45.0	‡	15.8	15.8 >167	6.4
თ	Spill parent compound-Right able	394.24	394.24 Removal of R2 and R3 1.1	R2 and R3	1.1	0.9	>254	l	>254	>254 142.3	r.

FIGURE 351

37.17		- 1			Rat	Ratio**			IC-50-M	IC-50-MTT uM *** Jurkatt	Jurkatt
ا خ	Structure	<u>×</u>	Modification	R group	100 ug/m!	25 ug/ml	IC-50 uM	100 ug/ml 25 ug/ml IC-50 uM Summ activity Jurkatt MCF-7	Jurkatt	MCF-7	IC-50 uM
10	Remove R3	477.31	Removal of R3	R3	1.5	6:0	>210	ı	128.8	150.0	T.N
1	Remove R3-Acery substitution (ethyr)	505.3	Replacement of R3 with ethyl	R3	2.2	1.7	49.5	‡	16.0	25.7	7.6
14	Remove urea 2-methyl substitution	506.36	Removal of N-urea	Urea.	2	1.8	43.4	‡	19.2	21.4	7.3
17	Remove ures 1-methyl substitution	506.36	Removal of N'-urea	Urea	1.7	1.4	175.8	+	16.0	10.0	L.N
18	Remove ureas-benzori substitution	581.36	Replacement of phenylurea with phenylacyl	Urea	8.	1.2	154.8	+	38.9	24.5	F.Z
19	Remove weas-acotylate	457.33	Replacement of phenylurea with acetyl	Urea	1.2	0.9	218.7	ı	127.9	87.4	L.N.
20	Urea substitution-etity i brocyanate	515.38	Replacement of phenylurea with ethylurea	Urea	9:1	-	194.0	-	92.8	>194	^30
21	C C C C C C C C C C C C C C C C C C C	639.41	Replacement of phenylurea with pmethylphenylurea	Urea	2.3	1.7	42.2	‡	32.1	>156	5.4
22	φ φ φ Ves substitution 4 thorophenylisocyanale	647.36	Replacement of phenylurea with pfluorophenylurea	Urea	Έ	1.5	55.6	‡	14.5	102.0	3.9
23	OF Social Control of C	701.35	Replacement of phenylurea with p-	Urea	9:1	1.2	>143	+	74.0	117.2	N.T.
					ĺ						

Caspase-XIAP derepression assay*:crude compounds/080603
Ratio** =Vmax compound+C3+XIAPV/max C3+XIAP
++: As active as native or not more than 20 % decrease
+: less active, ~30 % reduction
-:No activity at 100 ug/ml
MTT data***=activity for crude and pur compounds, pure ones are:11,12,13,14,15,16,20,21,22
11,12,13,14,15,16,20,21,22

FIGURE 35B (cont.)

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TPI1332	Structure	MW
	Ç= ₄₆	
		į
	َّ الْهُ الْهُ [L-Ala][L-Trp(CHO)][L-Trp(CHO)][L-ThiAla]	613.74
<u>, </u>		010.77
	W AND THE COLONIA COLONIA	040.40
2	[L-Ala][L-Trp(CHO)][L-Trp(CHO)][L-pClPhe]	642.16
	φ.,	
3	[L-Ala][L-Trp(CHO)][L-Trp(CHO)][L-Nal]	657.77
		
4	[L-Ala][L-Trp(CHO)][L-Trp(CHO)][D-Nal]	657.77
·		
5	[L-Ala][L-Trp(CHO)][L-Trp(CHO)][L-3I-Tyr]	749.61
	₹³ _{№5}	
6	[L-Ala][D-Trp(CHO)][L-Trp(CHO)][L-ThiAla]	613.74
	, ,	
7	[L-Ala][D-Trp(CHO)][L-Trp(CHO)][L-pClPhe]	642.16
<u> </u>	In wall the transfer to be to the	O 72. 10

FIGURE 36A

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TPI1332 Structure	MW
8 [L-Ala][D-Trp(CHO)][L-Trp(CHO)][L-Nal]	657.77
9 [L-Ala][D-Trp(CHO)][L-Trp(CHO)][D-Nal]	657.77
10 [L-Ala][D-Trp(CHO)][L-Trp(CHO)][L-3I-Tyr]	749.61
11 [L-Ala][D-Nal][L-Trp(CHO)][L-ThiAla]	624.76
12 [L-Ala][D-Nal][L-Trp(CHO)][L-pClPhe]	653.18
13 [L-Ala][D-Nai][L-Trp(CHO)][L-Nai]	668.80
14 [L-Ala][D-Nal][L-Trp(CHO)][D-Nal]	668.80

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058

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TPI1332	Structure	MW
1		
15	III. Alalin Nalii Tra(CHO)III. 31 Turi	760.63
15	[L-Ala][D-Nal][L-Trp(CHO)][L-3I-Tyr]	760.63
	H ₂ N	
16	[D-Trp(CHO)][L-Trp(CHO)][L-Trp(CHO)][L-ThiAla]	728.88
	H ₂ N ₂ O _{NH2} O _{NH}	
17	[D-Trp(CHO)][L-Trp(CHO)][L-Trp(CHO)][L-pClPhe]	757.29
18	[D-Trp(CHO)][L-Trp(CHO)][L-Trp(CHO)][L-Nal]	772.91
19	[D-Trp(CHO)][L-Trp(CHO)][L-Trp(CHO)][D-Nal]	772.91
	H ₂ N OH	·
20	[D-Trp(CHO)][L-Trp(CHO)][L-Trp(CHO)][L-3I-Tyr]	864.74
	H ₂ N S	
21	[D-Trp(CHO)][D-Trp(CHO)][L-Trp(CHO)][L-ThiAla]	728.88

Title: METHODS AND COMPOSITIONS FOR... Inventors: Reed et al.

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058

	-		_	_
O	~	/1	7	2.
7	n		4	

TPI1332	Structure	MW
	H ₂ M O I NH O I	:
22	[D-Trp(CHO)][D-Trp(CHO)][L-Trp(CHO)][L-pClPhe]	757.29
	H ₂ N O NH ₂	
23	[D-Trp(CHO)][D-Trp(CHO)][L-Trp(CHO)][L-Nal]	772.91
	H NH2	
24	[D-Trp(CHO)][D-Trp(CHO)][L-Trp(CHO)][D-Nal]	772.91
	H ₂ N OH	
25	[D-Trp(CHO)][D-Trp(CHO)][L-Trp(CHO)][L-3I-Tyr]	864.74
	H ₂ N NH ₂	
26	[D-Trp(CHO)][D-Nal][L-Trp(CHO)][L-ThiAla]	739.90
ļ	H ₂ N O NH ₂	
27	[D-Trp(CHO)][D-Nal][L-Trp(CHO)][L-pClPhe]	768.32
28	[D-Trp(CHO)][D-Nal][L-Trp(CHO)][L-Nal]	783.93

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058 97/123

TPI1332	Structure	MW
	H ₂ N NH ₂	
29	[D-Trp(CHO)][D-Nal][L-Trp(CHO)][D-Nal]	783.93
30	[D-Trp(CHO)][D-Nal][L-Trp(CHO)][L-3I-Tyr]	875.77
,	H,N H, NH, S	
31	[L-Cha][L-Trp(CHO)][L-Trp(CHO)][L-ThiAla]	695.89
22		704.04
32	[L-Cha][L-Trp(CHO)][L-Trp(CHO)][L-pClPhe]	724.31
į	H ₂ N NH	
33	[L-Cha][L-Trp(CHO)][L-Trp(CHO)][L-Nal]	739.92
	H ₂ N H ₂ NH ₂	
34	[L-Cha][L-Trp(CHO)][L-Trp(CHO)][D-Nal]	739.92
	H ₂ N H NH ₂	
35	[L-Cha][L-Trp(CHO)][L-Trp(CHO)][L-3I-Tyr]	831.76

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TPI1332	Structure	MW
	H ₂ N NH ₂	
36	[L-Cha][D-Trp(CHO)][L-Trp(CHO)][L-ThiAla]	695.89
	H ₂ N O H ₁ O D O D O D O D O D O D O D O D O D O	
37	[L-Cha][D-Trp(CHO)][L-Trp(CHO)][L-pClPhe]	724.31
	H ₂ N NH ₂	
38	[L-Cha][D-Trp(CHO)][L-Trp(CHO)][L-Nal]	739.92
	H ₂ N O NH ₂	
39	[L-Cha][D-Trp(CHO)][L-Trp(CHO)][D-Nal]	739.92
	H ₂ N OH	
40	[L-Cha][D-Trp(CHO)][L-Trp(CHO)][L-3I-Tyr]	831.76
	H ₂ N H NH ₂	
41	[L-Cha][D-Nal][L-Trp(CHO)][L-ThiAla]	706.91
42	[L-Cha][D-Nal][L-Trp(CHO)][L-pClPhe]	735.33

TPI1332	Structure	MW
	H ₂ N NH ₂	
43	[L-Cha][D-Nal][L-Trp(CHO)][L-Nal]	750.94
44	[L-Cha][D-Nal][L-Trp(CHO)][Ď-Nal]	750.94
	H ₂ N H ₂ NH ₂	
45	[L-Cha][D-Nal][L-Trp(CHO)][L-3I-Tyr]	842.78
46	[L-Ala][D-Trp(CHO)][L-Trp(CHO)][D-Trp(CHO)]	646.75
	Man A B A B A B A B A B A B A B A B A B A	
47	[L-Ala][D-Trp(CHO)][L-Trp(CHO)][L-ThiAla]	613.74
40	(I_Ala)(D_Tro(CHO))(D_Pha)(D_Tro(CHO))	607.71
40	[L-Ala][D-Trp(CHO)][D-Phe][D-Trp(CHO)]	607.71
49	[L-Ala][D-Trp(CHO)][D-Phe][L-ThiAla]	574.70

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058

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TPI1332	Structure	MW
	H ₂ N + H ₂ NH ₂	
50	[L-Ala][D-Cha][L-Trp(CHO)][D-Trp(CHO)]	613.76
	H ₂ N H NH ₃	
51	[L-Ala][D-Cha][L-Trp(CHO)][L-ThiAla]	580.75
52	[L-Ala][D-Cha][D-Phe][D-Trp(CHO)]	574.73
	H ₂ N NH ₂	
53	[L-Ala][D-Cha][D-Phe][L-ThiAla]	541.71
54	[L-Ala][D-ThiAla][L-Trp(CHO)][D-Trp(CHO)]	613.74
55	[L-Ala][D-ThiAla][L-Trp(CHO)][L-ThiAla]	580.73
	H, N O D D D D D D D D D D D D D D D D D D	
56	[L-Ala][D-ThiAla][D-Phe][D-Trp(CHO)]	574.70

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058

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TPI1332	Structure	MW
	H ₂ N NH ₂ S	
57	[L-Ala][D-ThiAla][D-Phe][L-ThiAla]	541.69
50		700.04
58	[L-Ala][D-pIPhe][L-Trp(CHO)][D-Trp(CHO)]	733.61
59	[L-Ala][D-pIPhe][L-Trp(CHO)][L-ThiAla]	700.60
	HAN THE	
60	[L-Ala][D-pIPhe][D-Phe][D-Trp(CHO)]	694.57
	H ₂ N +	-
61	[L-Ala][D-plPhe][D-Phe][L-ThiAla]	661.56
	H ₂ N H ₂	
62	[L-Nal][D-Trp(CHO)][L-Trp(CHO)][D-Trp(CHO)]	772.91
	H _M S	
63	[L-Nal][D-Trp(CHO)][L-Trp(CHO)][L-ThiAla]	739.90

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TPI1332	Structure	MW
:		
64	[L-Nal][D-Trp(CHO)][D-Phe][D-Trp(CHO)]	733.87
į	H ₂ N O NH ₂	
65	[L-Nal][D-Trp(CHO)][D-Phe][L-ThiAla]	700.86
66	[L-Nal][D-Cha][L-Trp(CHO)][D-Trp(CHO)]	739.92
67	[L-Nal][D-Cha][L-Trp(CHO)][L-ThiAla]	706.91
	H ₂ N T T T N ₂	
68	[L-Nal][D-Cha][D-Phe][D-Trp(CHO)]	700.88
60	[L-Nal][D-Cha][D-Phe][L-ThiAla]	667.87
09	r Helle-Lucia	007.07
70	[L-Nal][D-ThiAla][L-Trp(CHO)][D-Trp(CHO)]	739.90

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TPI1332	Structure	MW
71	[L-Nal][D-ThiAla][L-Trp(CHO)][L-ThiAla]	706.89
72	[L-Nal][D-ThiAla][D-Phe][D-Trp(CHO)]	700.86
	S NH ₂ O NH O NH	
73	[L-Nal][D-ThiAla][D-Phe][L-ThiAla]	667.85
74	[L-Nal][D-plPhe][L-Trp(CHO)][D-Trp(CHO)]	859.77
75	[L-Nal][D-pIPhe][L-Trp(CHO)][L-ThiAla]	826.76
	H,N , H , H	
76	[L-Nai][D-piPhe][D-Phe][D-Trp(CHO)]	820.73
		,
77	[L-Nal][D-plPhe][D-Phe][L-ThiAla]	787.72

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058

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TPI1332	Structure	MW
	HO THE STATE OF TH	
78	[L-3I-Tyr][D-Trp(CHO)][L-Trp(CHO)][D-Trp(CHO)]	864.74
	HO HO NH2	
79	[L-3I-Tyr][D-Trp(CHO)][L-Trp(CHO)][L-ThiAla]	831.73
	HO H	
80	[L-3I-Tyr][D-Trp(CHO)][D-Phe][D-Trp(CHO)]	825.71
	H ₂ N	
81	[L-3I-Tyr][D-Trp(CHO)][D-Phe][L-ThiAla]	792.70
	HO H	
82	[L-3I-Tyr][D-Cha][L-Trp(CHO)][D-Trp(CHO)]	831.76
20		700 7
83	[L-3I-Tyr][D-Cha][L-Trp(CHO)][L-ThiAla]	798.74
	HO NH ₂	
84	[L-3I-Tyr][D-Cha][D-Phe][D-Trp(CHO)]	792.72

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058

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TPI1332	Structure	MW
	HO HO NH ₂	
85	[L-3I-Tyr][D-Cha][D-Phe][L-ThiAla]	759.71
	HO HO NH2	
86	[L-3I-Tyr][D-ThiAla][L-Trp(CHO)][D-Trp(CHO)]	831.73
0.7		700 70
87	[L-3I-Tyr][D-ThiAla][L-Trp(CHO)][L-ThiAla]	798.72
	HO HO NH2	
88	[L-3I-Tyr][D-ThiAla][D-Phe][D-Trp(CHO)]	792.70
89	[L-3I-Tyr][D-ThiAla][D-Phe][L-ThiAla]	759.69
	HO NATIONAL PROPERTY OF THE PR	
90	[L-3I-Tyr][D-pIPhe][L-Trp(CHO)][D-Trp(CHO)]	951.60
	H ₂ N + H ₂ N + S	
91	[L-3I-Tyr][D-pIPhe][L-Trp(CHO)][L-ThiAla]	918.59

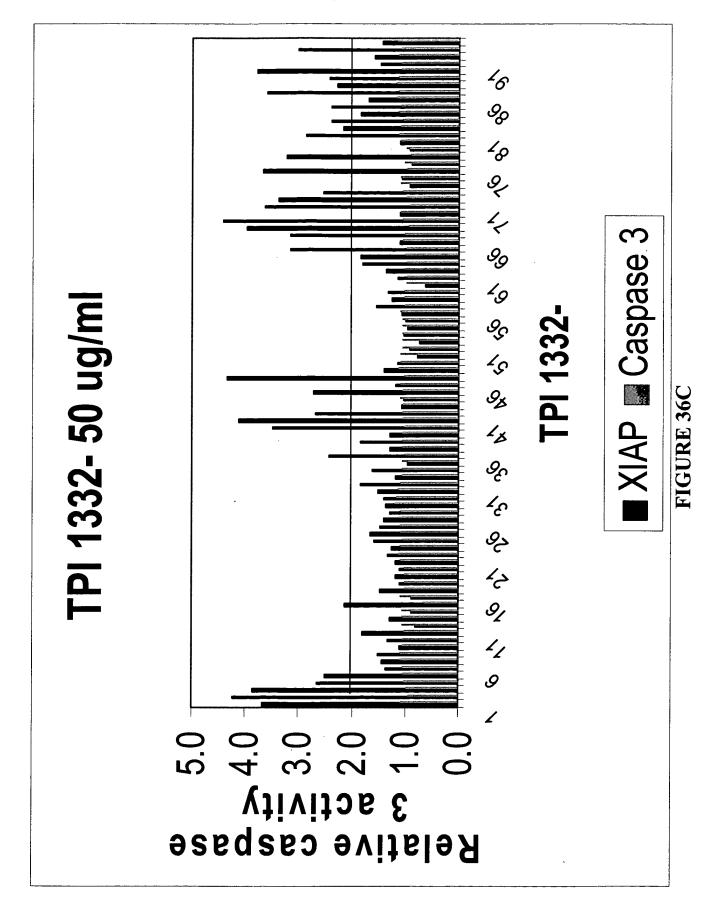
TPI1332	Structure	MW
•	HO H	
92	[L-3I-Tyr][D-pIPhe][D-Phe][D-Trp(CHO)]	912.57
·	HO HO NH2	
93	[L-3I-Tyr][D-pIPhe][D-Phe][L-ThiAla]	879.56

XIAP inhibitors-Tetrapeptides

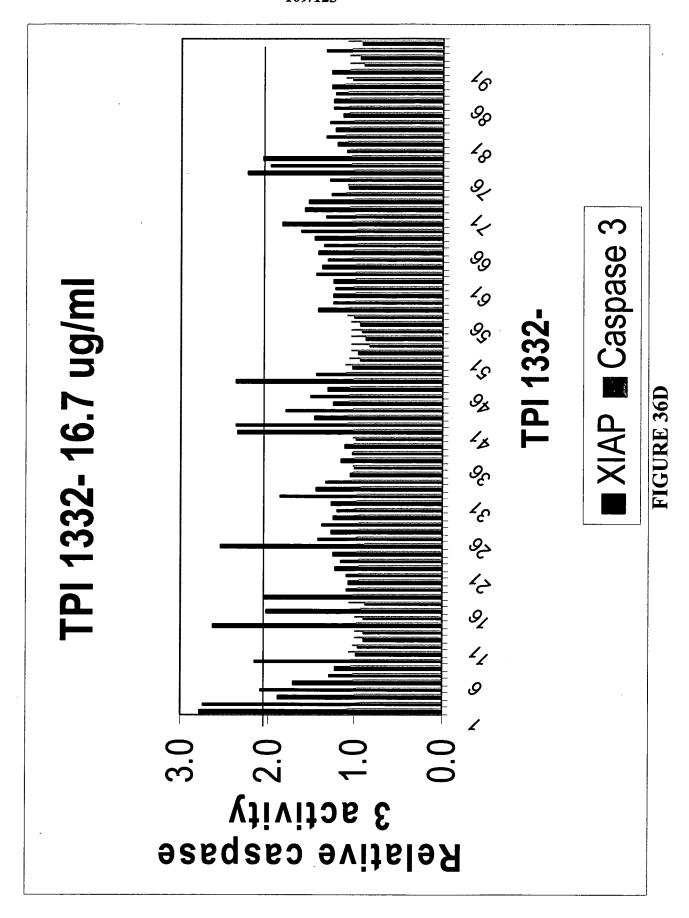
Competition assay Smac-7 mer/XIAP-BIR2

		Smac-7 mer/XIAP-BIR2 IC-50 uM		er/XIAP-BIR2
		MW	AVG	STD
TPI 1453-1 (TPI 792-33)	Exact Mass: 696.32793 [L-ThiAla]-[L-Nal]-[p-ClPhe]-[L-LyseFmoc]	900.9	48.4	10
TPI 1453-6 (TPI 792-35)	[L-ThiAla]-[L-Nal]-[p-ClPhe]-[L-LyseFmoc]	1068.8	12.6	4.8
TPl1332-4	(L-Ala)[L-Trp(CHO)][D-Nai]	657.8	3.9	3.6
TPI 1332-24	(D-Trp(CHO))[D-Trp(CHO))[L-Trp(CHO)][D-Nai]	772.9	5.0	4.8
TPI1332-41	[L-Chaj[D-Nai][L-Trp(CHO)][L-ThiAla]	706.9	48.5	0.9
TPI 1332-69	(L-Na[[D-Phe][L-ThiAla]	667.9	>150	
TPI 1332-76	(L-Nal][D-plPhe][D-Phe][D-Trp(CHO)]	820.7	36.2	20.9
TPI 1332-77	(L-Nal][D-plPha][D-Pha][L-ThiAla]	787.7	66.7	32.4
Smac 7-mer	AVPIAQK-NH ₂	724.4	18.8	4
Smac 4-mer	AVPI-NH2	397.2	30.3	

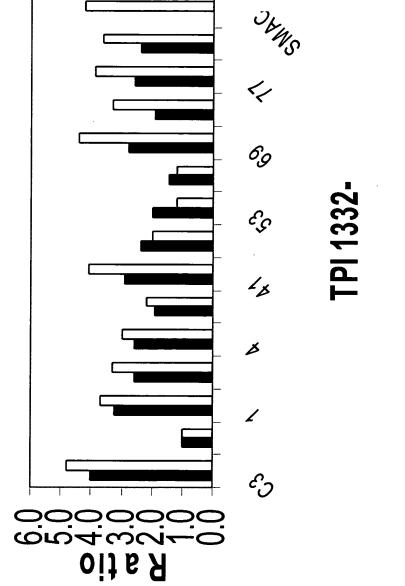
Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058



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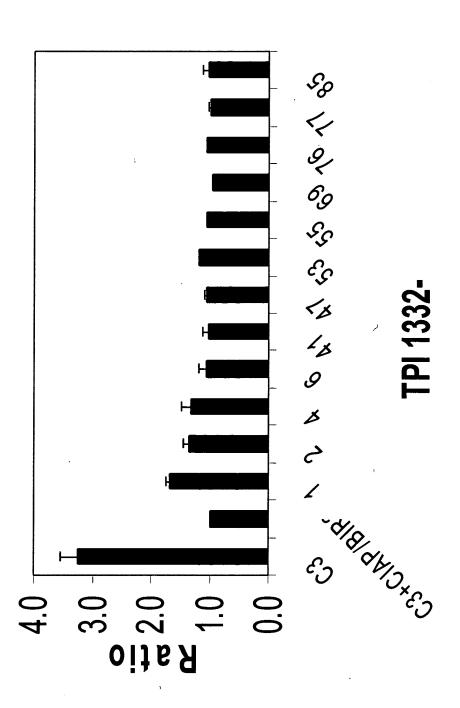
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■ XIAP-FL □ XIAP-BIR2

FIGURE 36E



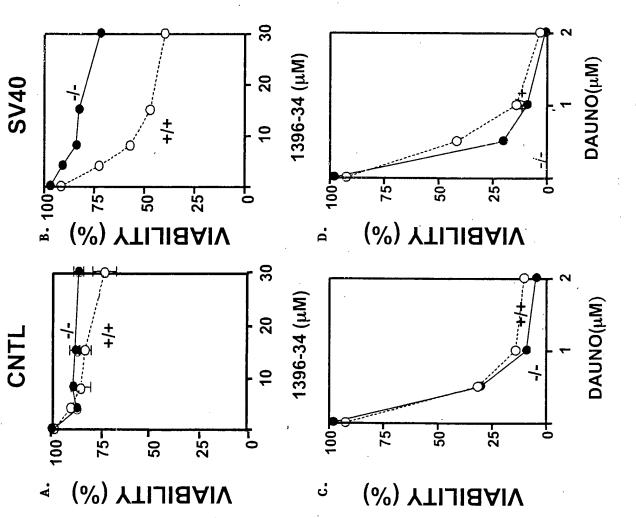


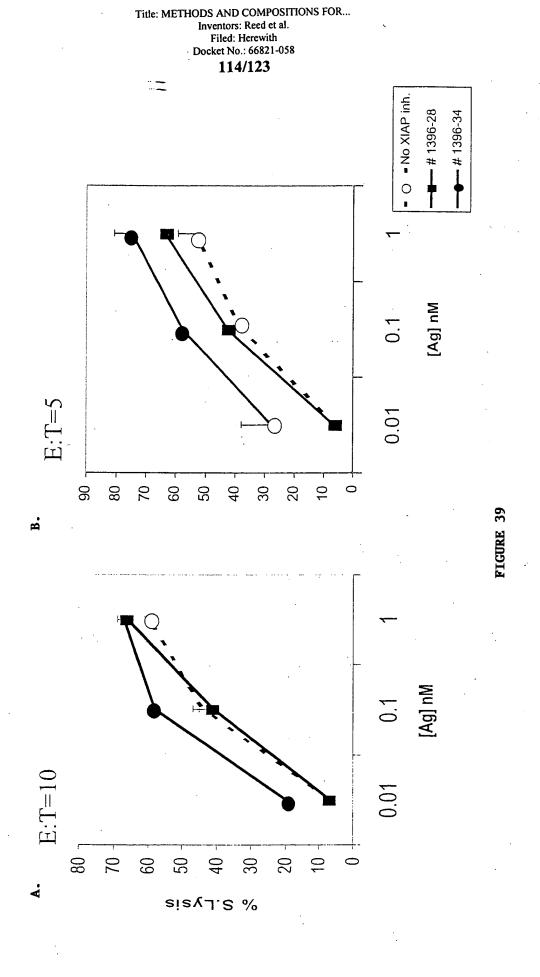
Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058 112/123

PI 1495-1 is the same	"	ıs TPI 1332-69	69-				XIAP-FL	Competitive	
							derepression	binding assay	
1495-						₹	IC20 nM	IC-50 uM	STD
÷	L-Nai	D-Cha	D-Phe	D-Phe L-ThiaAla -NH2		667.3	33.9	>150	
±	၁	D-Cha	D-Phe	D-Phe L-ThiaAla	-NH2	527.3	>189.7	>190	
Ŧ	L-Nal	9	D-Phe	D-Phe L-ThiaAla	-NH2	571.2	>175.1	>175	
Ŧ	L-Nal	D-Cha	5	L-ThiaAla	-NH2	577.3	>173.2	>175	
-H	L-Nal	D-Cha	D-Phe		-NH2	571.3	67.4	29.7	23.4
±	A	D-Cha	D-Phe	L-ThiaAla	-NH2	541.3	>184.8	>185	
±	L-Nai	A	D-Phe	L-ThiaAla	-NH2	585.2	>170.9	>170	
÷.	L-Nal	D-Cha	A	L-ThiaAla	-NH2	591.3	>169.1	>170	
+	L-Nal	D-Cha	D-Phe	4	-NH2	585.3	149.0	>170	
1237-Smac 7 mer	: 7 mer					724.4		18.8	4.0
1425- Smac 4 mer	: 4 mer					397.2		30.3	

FIGURE 37



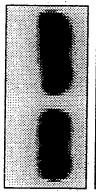




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Α.





CNTL

1396-12

actin

cleaved caspase-3

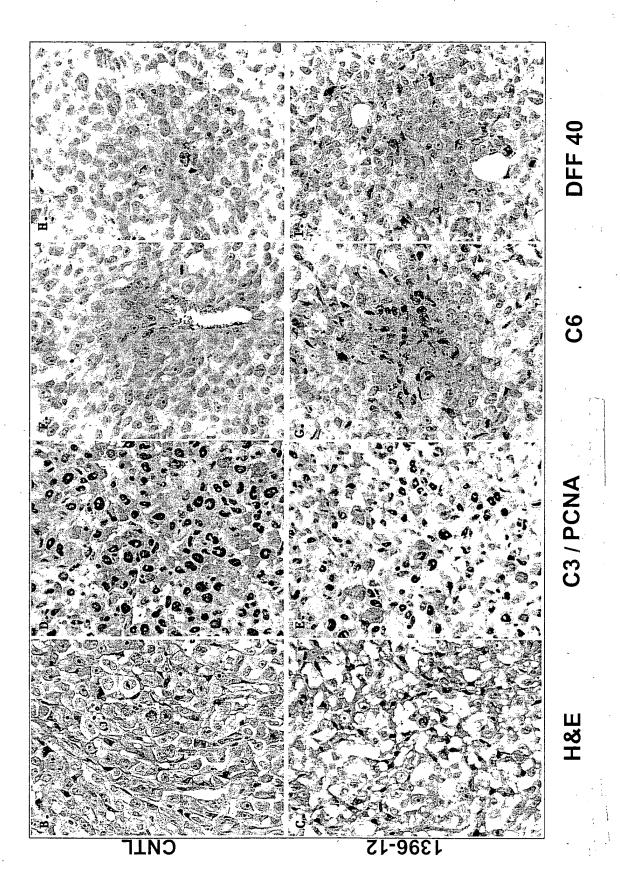


FIGURE 40 (cont.)

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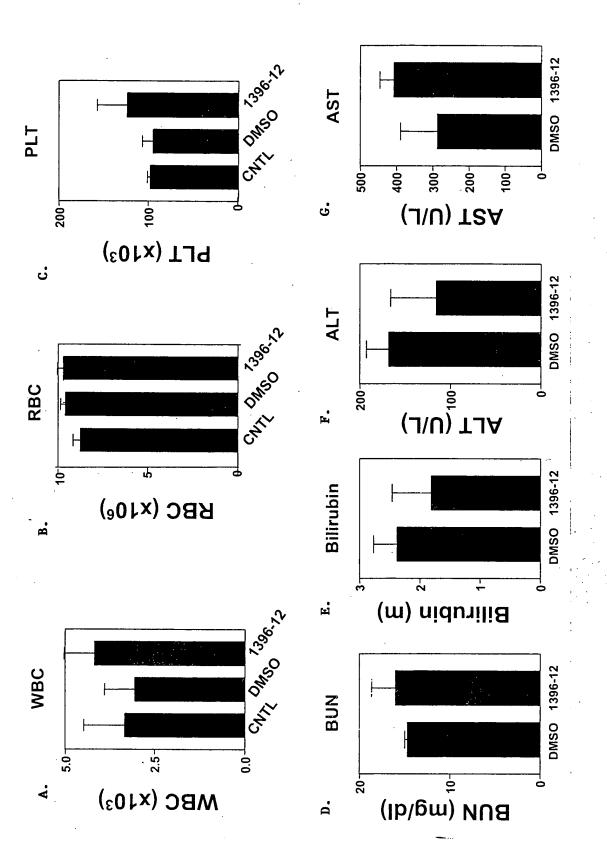


FIGURE 41

Title: METHODS AND COMPOSITIONS FOR...
Inventors: Reed et al.
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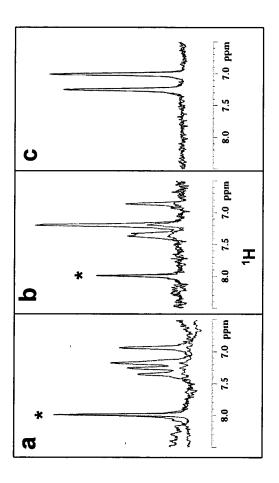


FIGURE 42

Title: METHODS AND COMPOSITIONS FOR... Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058 119/123

	STD	10.0	9.0	15.6	16.4	na	4.8	1.1	6.9	16.4	3.6	4.0	
Competitive binding assay	IC-50 uM	48.4	10.1	57.7	38.5	>165	12.6	4.2	7.1	38.5	3.8	18.8	30.3
fa	STD	10.3	9.0				2.1	16.7	1.7		8.6		
XIAP-FL derepression data	AVG IC-50 uM	21.0	14.1	~131.7	0.69	> 164.7	6.1	36.4	24.0	0.69	19.0		
XIAP-FL d	[lowest ratio 1.8]	12.5	6.25	~100	25	>100	3.13	6.25	3.13	25	6.25		
	× ×	6.006	803.7	759.5	775.2	607.3	1068.8	971.6	927.4	775.2	775.2	724.4	397.2
		-NH ₂											
		LyseFm	Lys eFm	Lys eFm	Lys eFm		Lys eFm	Lys eFm	Lys eFm	Lys eFm			
		pCI-L-f	pCI-L-f	pCI-L-f	ပ	pCI-L-f	dLysFm	dLysFm	dLysFm	5	dLysFm		
		L-Nal	L-Nal	Э	L-Nai	L-Nai	L-Nal	L-Nal	9	L-Nai	L-Nal	į	_
		L-Thiala	9	L-Thiala	L-Thiala	L-Thiala	L-Thiala	9	L-Thiala	L-Thiala	L-Thiala	TPI 1237- Smac 7 mer	PI 1425- Smac 4 mer
	TPI 1453	1	2	3	4	2	9	7	8	4	6	TPI 1237-	TPI 1425-

TPI 1453-1=TPI 792-33 and TPI 1408-3 TPI 1453-6=TPI 792-35

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		200	gednessee									
TPI 1554#	Non-Biotin Synthesis #		1	2	က	4	2	9	7		×	
TPI 1554-1	PI 1554-1 TPI 792-33, TPI 1408-3, TPI 1453-1	±	H- L-Thiala	L-Nai	pCI-L-f	Lys eFm	(Biotin	6aha)	Kboc/fmoc	-NH2	1365.6	
TPI 1554-2	TPI 792-35, TPI 1453-6	±	L-Thiala	L-Nal	dLysFm	Lys eFm	(Biotin	6aha)	Г	-NH2	1534.7	
TPI 1554-3	TPI 1332-4	÷	Boc-L-Ala	Boc-L-Trp(CHO)	Boc-L-Trp(CHO)	Boc-D-Nal	(Biotin	6aha)	Kboc/fmoc	-NH2	1124.5	
TPI 1554-4	TPI 1332-41	Ŧ	Boc-L-Cha	Boc-D-Nal	l	Boc-L-ThiAla	(Biotin	6aha)	Kboc/fmoc	_	1173.6	
TPI 1554-5	TPI 1332-69	Ŧ	Boc-L-Nal	Boc-D-Cha	l	Boc-L-ThiaAla		6aha)	Kboc/fmoc	-	1134.6	
TPI 1554-6	TPI 1332-77	±	Boc-L-Nai	Boc-D-pIPhe	Boc-D-Phe	Boc-L-ThiaAla	(Biotin	6aha)	Kboc/fmoc	-NH2	1254.4	
TPI 1554-7	TPI 1495-19	Ħ	L-Nal	pCI-L-f	Lys eFm	(Biotin	6aha)	Kboc/fmoc		-NH2	1212.6	
TPI 1554-8	TPI 1554-8 TPI 1495-20	±	L-Thiala	L-Nal	dLysFm	(Biotin	6aha)	Kboc/fmoc		₽-	1184.6	

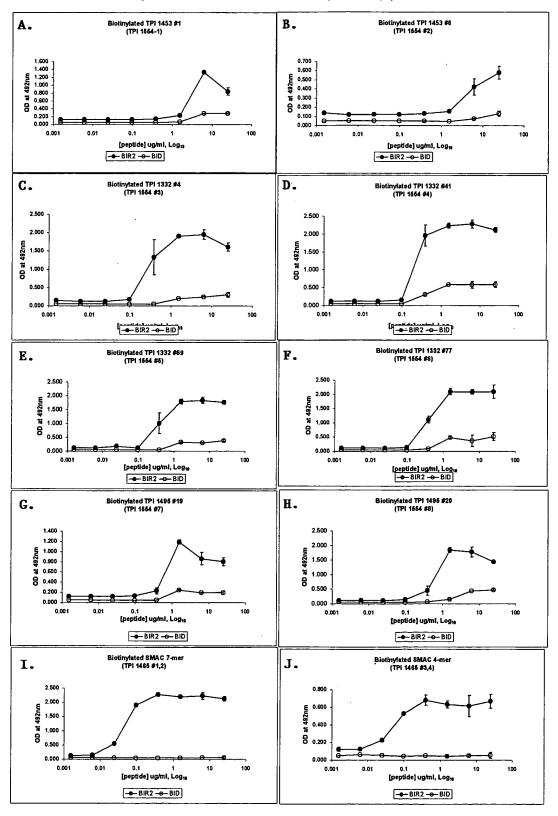
TPI 1554 Bi tinylated Tetrapeptides

FIGURE 44

Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058

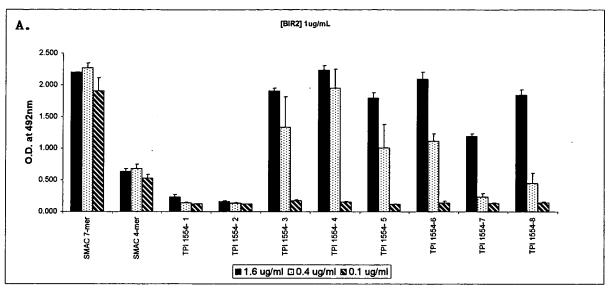
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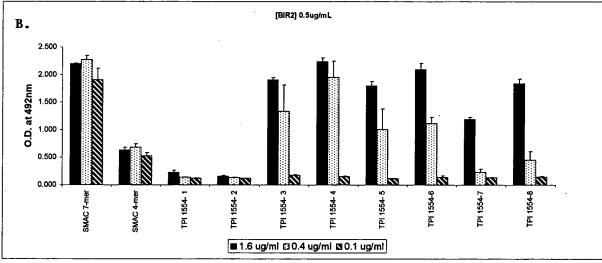
Binding of XIAP-BIR2-GST and BID-GST to Biotinylated Tetrapeptides

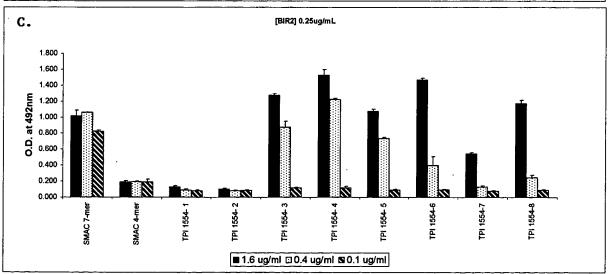


Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058 122/123

Three Concentrations of XIAP-BIR2-GST Binding t Biotinylated Peptides







Inventors: Reed et al. Filed: Herewith Docket No.: 66821-058 123/123

Comp tition for the Binding of Biotinylated Tetrapeptides with XIAP-BIR2-GST

